TEXT BOOK
OF PHYSIOLOG

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A

TEXT-BOOK

OF

PHYSIOLOGY.

BY

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TO HIS TEACHER

CARL LUDWIG

THIS BRIEF WORK

IS

DEDICATED

IN

REVERENCE AND GRATITUDE

BY

THE AUTHOR.

PREFACE.

PHYSIOLOGY is an experimental and superstructural science occupying a field quite as definite as Anatomy, Chemistry and Physics, the three foundations on which it is built. Though all physiologists impress these facts in their teaching, no volume has hitherto been based on the advantages of presenting the subject concretely within its own proper boundaries, and in its instructive connections with the sciences whence it is derived.

In approaching Physiology from this standpoint the author has summarized in the Introduction those principles of Physics and Chemistry which have a general application, and has prefixed to each chapter an abstract of the facts drawn from all three of the basic sciences which are to be applied in the succeeding text. This method possesses the obvious teaching value of confining the subject-matter of each chapter strictly to Physiology and presenting it in logical relations.

The plan of the work adapts it to the needs of several classes of readers. Medical students will, it is hoped, find a clearly defined exposition of Physiology proper, its relevant facts from Chemistry, Physics and Morphology, and accompanying outlines enabling them to arrange their knowledge in an orderly and logical manner. Students in literary or scientific institutions who are preparing for the study of medicine or of physiology as a specialty, will find the method of the book equally adapted to their needs, inasmuch as the general and special introductions review matter which has been the subject of detailed study in the laboratories of Physics, Chemistry and Biology, and which forms the basis of Physiology.

The same reasons render the method of the book convenient for the practitioner. The style is as brief and concise as compatible with the needs of students, and space has thereby been gained for the inclusion of clinical applications of physiological facts and principles.

Readers interested in physiological chemistry will find the structural formulas and reactions of the complex bodies involved in physiology worked out in as much detail as the present status of chemistry will allow. The newer literature of this subject is noted in references.

Though the volume embodies original work on the part of the author, free use has been made of the great heritage of physiological knowledge without which no adequate presentation of the subject would be possible.

The author wishes to express here his obligations to Professor Piersol for the use of many of his excellent histological illustrations; to Professor E. B. Wilson for the use of several fine figures from his work on *"The Cell in Development and Inheritance"*; and to Professor Waller for several valuable engravings from his *Text-book of Physiology*. Several authors have contributed one or two figures each. Many have been taken from my *Laboratory Guide in Physiology*.

In the preparation of the text the author wishes to acknowledge his indebtedness to his associate, Professor W. K. Jaques, for much valuable material on the subject of *The Blood*, especially for Plates I. and II. showing varieties of red and white corpuscles; to Dr. Achard, a former pupil of Professor Bowditch, for the excellent contribution on *Internal Secretions*. The chapter on the physiology of the *Central Nervous System* was prepared by my associate, recently deceased, Dr. P. L. Holland, Instructor in Clinical Neurology. For the proof-reading and for many valuable additions to this chapter I am indebted to my associate, Dr. C. L. Mix, Instructor in Anatomy and Physiology of the Nervous System.

WINFIELD S. HALL.

CHICAGO, July, 1899.

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PHYSIOLOGY.

INTRODUCTION.

A. THE SCOPE OF PHYSIOLOGY AND THE PROBLEMS WITH WHICH IT DEALS.

1. DEFINITIONS.

PHYSIOLOGY treats of the functions of different tissues and organs of living organisms. Living organisms are divided into plant and animal kingdoms, so there is *Plant Physiology* and *Animal Physiology.* It has been customary to subdivide the latter into *Comparative Physiology,* treating of the ways in which the different functions—digestion, circulation, etc.—are performed in the different classes of animals, and *Human Physiology,* treating of the special physiology of man. Another subdivision of the subject is into *General Physiology,* treating of the general functions of cells and tissues, and *Special Physiology,* treating of the special functions of organs and systems of organs.

Defined in more general terms,—*Physiology is the science of the phenomena of living nature.* Reduced to its final elements, a natural phenomenon always involves matter and energy. A general knowledge of the properties of matter and of energy is of great importance to him who would study the phenomena of life.

2. MATTER.

All of the substance or material in the universe, which appeals to our senses, has weight and resistance, and is called *ponderable matter,*—it may be weighed in a balance. It is with this form of matter alone that physiology deals. Physicists, chemists, and astronomers find it a necessity to assume the existence of another form of matter.

This other form of matter fills all space not actually occupied by atoms of ponderable matter; it transmits the sun's heat and light to us through space. This form of matter cannot be weighed in a balance, and is called *imponderable matter.*

- Matter
  - Ponderable
    - As to aggregate condition
      - Solid.
      - Liquid.
      - Gaseous.
    - As to units of division
      - Indefinite.
        - Mass
        - Particle
      - Definite.
        - Molecule
        - Atom
  - Imponderable.

Physiological problems involve ponderable matter in some of the forms indicated and under the influence of energy.

3. ENERGY.

Energy is the capacity or power to do work. This capacity for power to do work may be manifested or not. We speak of the pent-up energy of a charge of gunpowder, also of the tremendous energy of the explosion ; we speak of a man of energy, but we do not expect the man to manifest his energy constantly. This dual idea of energy is expressed in its classification as *potential* energy and *kinetic* energy ; *i. e.*, *latent* and *active* energy. Energy is further classified as to its nature. That form of energy most universal in its influence is gravitation : according to the law of gravitation, "Every particle of ponderable matter in the universe attracts every other particle with a certain force."

a. The Transformation of Energy.

The changes above mentioned, by which potential energy may be changed into kinetic energy, is not a transformation in the sense here intended,—it is simply a liberation of latent energy, whereas the reverse operation would be a making latent of active or kinetic energy.

By the Transformation of Energy quite a different process is indicated. If one hold an object in an elevated position, and release it, it falls to a position of equilibrium. The motion of the mass is lost but the shock of impact has transmitted the motion of the mass to the physical and chemical units of the mass—the atoms—and this atomic vibration appeals to our senses not as motion, but as heat. The energy of mass or molar motion is thus transformed into the energy of atomic motion or heat. The intensity of atomic motion may be so great, *i. e.*, the heat may be so great, that the vibrations appeal not only to our temperature sense as heat, but also to our eyes as light. Still another form, into which energy may be transformed, is electricity. Thus gravitation is a general and ultimate form of energy which may undergo various transformations.

Another ultimate form of energy, especially manifested in the form of heat, light, or electricity, is chemical affinity. By virtue of molecular attraction every molecule of matter is attracted by every other molecule in proportion to their respective masses, and with a force varying inversely as the square of the distance between them, irrespective of the kind of matter; but, by virtue of a peculiar affinity between atoms of certain different kinds of matter, these atoms are drawn into new and most intimate contact, manifested by heat or light or electricity, and resulting in a new combination of matter, having physical properties different from those of either constituent. This kind of energy, and its transformation forms, are of the most fundamental importance to physiology; and constant reference must be made to them.

Matter is transformable, but is not destructible. Energy is transformable; is it destructible? Matter may be so transformed as to make it useless to man, *i. e.*, lost to use, but not destroyed; in the same way energy may be dissipated into space but not destroyed. This great fact was discovered, and demonstrated by Julius Mayer, and by Helmholtz, and may be looked upon as the most important advance of physical science during this century. It is called the law of the conservation of energy.

b. Law of the Conservation of Energy.

Ganot expresses this law as follows: "The total amount of energy possessed by any system of bodies (*e. g.*, the solar system) is unaltered by any transformations arising from the action of one part of the system upon another, and can only be increased or diminished by effects produced upon the system by external agents."

The experimental proof of the truth of this law involves the reduction of all forms of energy to units. The unit of heat energy, called the *calorie* or gramme-calorie, is that amount of heat required to raise one gramme of water one degree of temperature. If it is required to reduce units of motion to units of heat one has only to remember that experiment has proven that 425.5 grammes, falling through a distance of one meter, would, by impact with an absolutely resistant surface, generate enough heat to raise the temperature of 1 gramme of water 1° Centigrade. This is known as the *Mechanical Equivalent of Heat.* The principles involved in the transformation of energy, and the conservation of energy, are fundamental, and we shall presently see their inestimable importance in any clear conception of the phenomena of living nature. All natural phenomena involve matter and energy. The phenomena of living nature can differ from those of lifeless nature only in the matter or in the energy involved. We are at once brought face to face with the most difficult problem of Physiology —the abstract differentiation between the living and the lifeless.

Let us approach this subject by an enumeration of the kinds of matter of which living beings are composed. It was formerly supposed that an analysis of the animal body would reveal chemical elements peculiar to living bodies. Chemistry has, however, established no fact more thoroughly than that the animal, or plant, body contains no new kinds of matter. Analysis shows the presence of carbon, hydrogen, nitrogen, oxygen, sulphur, phosphorus, chlorine, and of sodium, potassium, calcium, magnesium, iron—occasionally traces of silicon, manganese, fluorine, lithium, bromine, and iodine are found. These are the most common elements in the surface of the earth. After finding that living nature differs in no way from non-living nature as to the kinds of matter involved, the physiologist turned to the investigation of the kinds and forms of energy, expecting to find associated with life a new energy. Until quite recently, most physiologists, since the time of Johannes Müller, have believed that the energy manifested in living nature is identical with that manifested in non-living nature, and, further, that it obeys the same laws of transformation in living as in lifeless bodies. This belief was based upon observation in a large number of physiological phenomena. For example, it has been demonstrated that the heat and mechanical energy which an animal may expend is exactly equivalent to the potential energy represented by the food which the animal absorbs. There remain, however, many unsolved problems regarding the energy involved in absorption, secretion and excretion. The more these problems are studied, the clearer seems to be the indication that energy may undergo, in the animal or plant organism, a transformation not observed outside of living organisms. Along with this indication comes repeated and indubitable proof that, whatever transformations energy may undergo within the living organism, the quantity of energy that leaves the organism, dissipated into space as heat or motion, is exactly equal to the quantity that enters the organism as potential energy. Whatever may be said about vital energy, it is certain that it does not mean that any new energy is created by living organisms.

In discussing the matter involved in living organisms, the elements which occur in living bodies were enumerated, but the study of the combination of these atomic elements into molecules was omitted. In lifeless nature we find as typical molecules, H_2O, CO_2, $CaCO_3$, $MgCO_3$, $NaCl$, $CaSO_4$, KNO_3, Fe_2O_3, PbS, etc.

These typical compounds, which make up a large proportion of the earth's crust, are composed each of three to six atoms of two to three kinds of matter. There are, however, in the realm of inorganic nature, some very large and complex molecules, *e. g.* :—

Crystalline ammonic ferric alum $Fe_2(SO_4)_3(NH_4)_2SO_4+24H_2O$. This complex molecule contains 104 atoms, and has 962 times the weight of H. One of the simplest molecules met among the products of life is the glucose molecule ($C_6H_{12}O_6$), whose 24 atoms weigh 180 times as much as an atom of hydrogen. Egg albumen was given by Hofmeister the formula: $C_{204}H_{322}N_{52}O_{66}S_2$; its 646 atoms weigh 4,618 times as much as hydrogen. Zinoffsky determined the formula for the hæmoglobin of the horse's blood corpuscle to be: $C_{712}H_{1130}N_{214}FeS_2O_{425}$. This prodigious molecule has 2,304 atoms and a molecular weight of 16,710. Here we have struck the key-note of the difference between living and lifeless nature. *In its composition, living matter differs from lifeless matter not in the kind of material elements but in the complexity of the combinations.* A similar course of reasoning, applied to the energy, would result in the conclusion that: *The energy involved in the phenomena of living nature differs from the energy involved in the phenomena of lifeless nature only in the complexity of the transformations.*

4. LIFE.

Having now determined the essential difference between living and lifeless nature as to the matter and energy, let us investigate the nature of life in the abstract. Compare a dead with a living organism; take, for example, a frog just dead. We observe a cessation of activity, *i. e.*, a cessation of manifest energy. The breathing movements cease, the heart ceases to beat, the animal ceases to take food; it becomes cold; if we stimulate it there is no response; in a few hours disintegration of the material begins. How shall we interpret this change? The activities which have ceased were the activities which adjusted the animal to its environment; built up its tissues from its food; and brought a continuous supply of oxygen to enter into combination with the tissues, and liberate the energies which were manifested in the phenomena of life. With the loss of life has been lost the energy necessary to adjust the internal needs of the body to the action of the environment. Herbert Spencer defines life as "*The continuous adjustment of internal relations to external relations.*" Though this reasoning and the explanation clear our conception of life somewhat, still life remains, and will long remain a mystery. A concrete idea of the typical phenomena of life may best be gained from the observation of a living organism.

5. A LIVING ORGANISM.

Such an organism begins its life as a minute globule (cell) of sensitive, spontaneously moving matter (protoplasm). The original volume is always increased (growth) by addition of matter from within (intussusception). Having attained a certain maximum of volume (maturity) the organism retains essentially the same volume for a time (adult life), and finally divides into equal or unequal parts (reproduction), the parts divided off beginning again the cycle of life, reaching, at maturity, a form always resembling the parent organism in form and activity. During the whole period of life there are certain activities which are manifestations of energy, liberated within the organism through a process analogous to a combustion of tissue (respiration,—destructive metabolism), which tissue is regenerated by the building up in the tissue (constructive metabolism) of elements or compounds taken in as food, dissolved (digestion), and carried to the wasted tissues (circulation). After growth is completed, and reproduction consummated, the wasting of the organism progresses faster than the regeneration (period of senility), and finally, the internal relations (needs) fail to be adjusted to the external relations (conditions of environment), and the organism ceases to live (death).

McKendrick ("General Physiology," p. 31) gives the following valuable recapitulation of the essential characters of a living being:—

(*a*) Molecular complexity; heterogeneity of parts, and chemical instability of the organic compounds forming it.

(*b*) Waste, and incessant repair of organic materials.

(*c*) The conversion of kinetic into potential energy, as the framework of the body is built up, or stores of reserve material are formed.

(*d*) Liberation of kinetic energy in various modes, and, in particular, as mechanical movement, heat and electricity.

(*e*) Organization, or the adaptation of certain parts of the body to particular functions.

(*f*) A regular evolution from origin of death.

(*g*) Origin from a parent, and the possibility of producing the elements of offspring.

(*h*) A power of variability and of adaptation to external conditions.

Physiology deals with the problem of NUTRITION; including *digestion, absorption, respiration, circulation, constructive* and *destructive metabolism, secretion* and *excretion;* with the problems of MOTO-SENSORY ACTIVITY, including the functions of the motor and nervous systems of the special senses; and, finally with the problems of REPRODUCTION.

B. THE RELATION OF PHYSIOLOGY TO THE OTHER NATURAL SCIENCES.

THE NATURAL SCIENCES.

- **The Physical Sciences.**
  - *Chemistry.*
  - *Physics.*
  - *Astronomy.*
  - *Geology.*
- **The Biological Sciences.**
  - MORPHOLOGICAL.
    - 1. *Anatomy.* Science of living forms.
      - Gross.
      - Minute.
        - Plant or Animal.
    - 2. *Paleontology.* Science of fossil forms.
      - Paleophytology.
      - Paleozoölogy.
  - PHYSIOLOGICAL.
    - 1. *Physiology.* Science of functions of living organisms.
      - General.
      - Special.
        - Plant or Animal.
    - 2. *Psychology.* Science of psychic phenomena.
      - Comparative.
      - Human.
    - 3. *Pharmacology.* Science of the action of drugs.
      - Comparative.
      - Human.
  - MORPHO-PHYSIOLOGICAL.
    - 1. *Embryology.* Science of Development of structures and functions.
      - Comparative.
      - Special.
        - Plant or Animal.
    - 2. *Pathology.* Science of diseased forms and functions.
      - Comparative.
      - General.
      - Special.
        - Plant or Animal.
    - 3. *Anthropology.* The Biology of Man.
      - *a.* Physical Anthropology. The Animal, Homo.
      - *b.* Ethnology. Races of Homo sapiens.
      - *c.* Ethnography. Geographical distribution of the races.

C. THE DEVELOPMENT OF PHYSIOLOGY AS A SCIENCE.

HISTORICAL REVIEW.

5th B.C.	**Antiquity.**	Heracles and Empedocles (500 B.C.). Hippocrates (460 B.C.).
4th B.C.		Aristotle (384 B.C.).
3d B.C.		Erasistratus (280 B.C.).
2d B.C.		
1st B.C.		
A.D. I.	**Early Christian Era.**	
II.		—131 } —200 } Galen.
III.		
IV.		
V.		
VI.	**Middle Ages.**	
VII.		
VIII.		
IX.		
X.		
XI.	**Dark Ages.**	
XII.		
XIII.		
XIV.		
XV.		Paracelsus (1490).
XVI.	**Modern Times.**	Servetus (1511).
XVII.		Harvey.
XVIII.		Haller.
XIX.		Müller. Wöhler, Hoppe-Seyler, Brüke, Liebig, Bunge, Ludwig, Voit, Hammersten, DuBois-Reymond, Pflüger, Halliburton, Marey, Zunst, Bernard, Kühne, Weber, Hering, *et al.*

The first traces of vague physiological conceptions are lost in the impenetrable darkness of prehistoric times. These vague conceptions find expression in mythology. In mythology there is no classification of knowledge: all knowledge being made to do homage to higher beings or deities, and this sum of human knowledge, as it existed in prehistoric times, must be looked upon as an indivisible whole from which, in the lapse of centuries, there gradually crystallized out: theology, philosophy, medicine, and natural science. In this mythological period life was characterized by motion. Wind, water, fire, stars, sun, and moon were personified. In historic times the first traces of a science based upon observation was, curiously enough, metaphysics or psychology.

This first attempt at biological science laid as the cornerstone of its foundation the proposition, "The human being is dual—the physical and the psychical—the body and the soul," and rounded its dome with the theory of metempsychosis, or wandering of the soul. From India this system of philosophy gradually made its way through Egypt to Greece, where it was championed by Pythagoras. It is remarkable that many of the philosophers of antiquity promulgated theories which are again, after a lapse of twenty-five centuries, forming the foundations of modern science. This is especially true of the theories regarding the origin and development of living nature. *Anaximander* (620 B. C.) believed that man descended from animal-like progenitors, who originally lived in water. *Heracles* (500 B. C.) had a conception of the "Struggle for Existence." *Empedocles* (504 B. C.) believed that, in the realm of living nature, plants originated first, then lower animals, then higher animals, and finally man. He believed that the active factor in this development was the destruction, in their *struggle* for *existence*, of the animals unfavorably constructed, while those capable of survival propagated the species, and transmitted their favorable structures. In the fifth century B. C. *Hippocrates* systematized medicine and founded the *Regular School.* His additions to knowledge were unimportant in Morphology and Physiology. His materia medica, Therapy, and practice of medicine were incomparably superior to what had preceded, and stood unimpeached for six centuries. In the fourth century B. C. *Aristotle,* the great observer of the phenomena of living nature, and the great collector of facts, laid the first enduring foundation for the *biological sciences.* In the third century B. C. *Erasistratus,* of the Alexandrian school, was the first to attempt a philosophy of physical life—a theory of physiology. He gave definite form to a theory, which had its origin among the pupils of Plato, and which reached its highest development under Galen and his school. This theory is called the *Pneuma Theory,* and, according to it, the Pneuma zotikon—life-giving spirit, or breath of life—resided in the heart, while the Pneuma psychikon—the soul—resided in the brain. Medical science having taken definite and authoritative form under Hippocrates, and physiology having been crystallized by the Pneuma theory of Erasistratus, there was a lapse of 400 years before there appeared the spirit who was destined to dominate the medical profession for more than thirteen centuries.

GALEN.

In the second century A.D. Galenus, a surgeon in the Roman army, made systematic dissections of the bodies of apes and other animals. Galen realized that medicine and surgery could not succeed unless based upon an exact knowledge of the structure of the body, and upon a knowledge of the vital functions; and, to the end last named, he performed vivisections upon apes and pigs, establishing the functions of the vagus, or pneumogastric nerve, and the intercostal nerves, and the effects of section of the spinal cord. After collecting a great mass of morphological and physiological knowledge he founded a *system of medicine.* His system of physiology was based upon the Pneuma theory, which, briefly expressed, was: *Pneuma psychikon*—the soul—resided in the brain and nerves, and presented the psychic phenomena, thought, sensation, and voluntary motion; *Pneuma zotikon*—life-giving spirit, or breath of life—entered the body through the lungs, resided in the heart, and expressed itself in heart-beat, pulse, and bodily warmth; while the *Pneuma physikon* resided in the abdomen, and presented the functions of nutrition, growth, secretion, and reproduction. No subsequent Roman even approached the colossal work of Galen, so it is easy to understand that, after the fall of Rome, his was the only authority recognized until the new birth—the renaissance—of art, literature, philosophy, religion, and science, in the fifteenth and sixteenth centuries. If, in all those thirteen centuries, any man doubted the statements or theories of Galen, he did not publish it, for Galen's authority was unimpeachable. The first recorded combatant of Galen was *Paracelsus* (1493 A.D.). Though he founded an untenable theosophistic philosophy, the simple fact of his impeachment of Galen's theories set the scientific world thinking. The feature of his system was, Unity in Nature; Nature a macrocosmus, and Man a microcosmus. Early in the sixteenth century *Vesalius, Eustachïo* and *Falloppia,* through dissection, extended the knowledge of anatomy; while *Servetus* disproved Galen's statement that the blood goes directly from the right heart to the left heart, and *Argentieri* contended that the blood nourished the tissues of the body. These advances prepared the way for the next great light in the renaissance of science.

HARVEY. (1578–1659.)

This great experimenter and observer was taught by his predecessors that the blood was in motion within the arteries and veins, and that the heart movements were the cause of this motion, but it remained for him to demonstrate that the arteries and veins were connected by smaller vessels (though, through lack of a microscope, he never saw them), and that the blood circulated within a closed system of tubes from the left heart through the arteries and capillaries, and back through veins to the right heart, thence to the lungs, and completed the circuit by entering the left heart. Next to this great triumph stands that notable proposition, first formulated by Harvey, "*Omne vivum ex ovo.*" The history of this proposition is most interesting. Twice it has been refuted, and twice the fallacies of the refutation have been demonstrated. Established at first on an observation of higher plants and animals, it was combatted by the early microscopists, who found, in their nutrient infusions, a rapid development of infusorian life with no discoverable eggs or germs. A century later Treviranus proved the fallacy of this "*Spontaneous Generation*" theory through the discovery of the real method of reproduction of these organisms; so the theory that "*all life is from an egg*" had stood its first assault. The improvement of the microscope, however, revealed the microbe. Nutrient fluids were seen to be soon swarming with life; the *Spontaneous Generation* theory was again revived, Harvey's theory again combatted; Pasteur has, however, in recent times, with his more exact instruments and methods, established, experimentally and conclusively, the verity of Harvey's proposition, "*All life is from an egg.*"

The microscope has been mentioned. It was in the latter part of the seventeenth century that Van Dyke and Leeuwenhoek invented the compound microscope, and *Leeuwenhoek*, with *Malpighi* and *Schwammerdamm*, made rapid strides in histological research. Up to the beginning of the eighteenth century, physiology had not been a separate and independent science.

HALLER.

It was Haller who, by his power of systematizing and generalizing, collected the facts peculiarly physiological, and constructed them into his renowned work, "*Elements of the Physiology of the Human Body.*" But Haller was, unfortunately, a philosopher rather than a philosophical investigator. He promulgated two theories which have had a retarding effect on Physiology; viz., *The Preformation Theory* and the *Theory of Vital Energy.* According to the first theory the *form of the organism existed in the egg*, and *embryological development* was simply *increase* in *size;* while.

according to the second theory the *Energy of Life*, is peculiar to life, *i.e.*, not transformable from physical and chemical energy, and, for that reason, called *Vital Energy*. This theory of a peculiar Vital Energy has retained a most tenacious hold on Physiology, and only through the combined efforts of a galaxy of experimenters in the first three-fourths of this century has the theory that the energy manifested in the phenomena of life is peculiar to life been abandoned. For a time it was hoped that all of the phenomena could be accounted for in the usual transformation forms of energy. More exact and extended recent experimentation makes it evident that there is a transformation form of energy peculiar to life. The living organism is not believed to be able to make energy, but simply to give it a new and unexpected form under certain circumstances. It is important to note, in this connection, that this newly discovered form of energy obeys, with the other forms, the law of the conservation of energy.

At the end of the eighteenth century *Priestly* and *Lavoisier* discovered *oxygen*. *Girtanner* demonstrated that it is this constituent of the atmosphere which, in the lungs, effects the change between venous and arterial blood.

JOHANNES MÜLLER.

The spirit which inspired and dominated physiological investigation during the first half of this century was Johannes Müller. Though he believed in a special Vital Energy, he believed that it followed implicitly the laws of energy in physics and chemistry, and set about, with physical and chemical methods, to investigate the phenomena of living nature. Johannes Müller was an indefatigable worker, an accurate and exact observer, a broad and judicious generalizer, and a profound philosopher. He was master of the whole field of Morphology and Physiology as it existed at the beginning of this century. He founded the new sciences of *Comparative Physiology* and *Physiological Psychology*, and laid for modern experimental Physiology the broad and deep foundations which have sustained the great superstructure erected by his pupils and successors during the last four decades. Soon after his death physiology was divided into *chemical* and *physical* physiology. The physiological chemists of this century are Wöhler and Liebig; Voit, Pflüger, and Zunst, Kühne, Hoppe-Seyler, Hammarsten, Bunge, and Halliburton, Chittenden and Atwater.

The investigators in the field of physical physiology are, first of of all, Ludwig, Weber, DuBois-Reymond, and Brücke; then Marey, Claude Bernard, Helmholtz, Hering, Hitzig, Goltz, Preyer, *et al.* Inasmuch as frequent reference must be made to these men during the course of our study, a detailed account of each man will not be entered upon here.

The great discoveries of this century, which have been of the greatest importance to physiology, are: (I) The *Law* of the *Conservation* of *Energy*; (II) The *discovery* of the *cellular structure* of *animal organisms*; (III) The discovery of the genealogy of the organic world; *i.e.*, *The establishment of the Evolution Theory.*

These three great principles have already been of inestimable value to physiology, but their service has only just begun.

PART I.

GENERAL PHYSIOLOGY.

CHAPTER I.

THE PHYSIOLOGY OF THE CELL: CYTOLOGY.

A. LIVING SUBSTANCE: PROTOPLASM.

1. THE PHYSICAL PROPERTIES OF PROTOPLASM.
2. THE CHEMICAL PROPERTIES OF PROTOPLASM.
3. THE MORPHOLOGY OF LIVING SUBSTANCE.
    - *a.* THE STRUCTURE OF PROTOPLASM.
    - *b.* THE STRUCTURE OF THE CELL.
        - (1) *Cytoplasm.*
        - (2) *The Nucleus; Nucleoplasm.*
        - (3) *The Centrosome.*
    - *c.* FORM AND SIZE OF THE CELL.
4. THE INDIVIDUALIZATION OF LIVING SUBSTANCE.

B. THE PHENOMENA OF LIFE.

1. NUTRITION.
    - *a.* ABSORPTION AND EXCRETION.
    - *b.* METABOLISM.
        - (1) *Chemical Phases.*
        - (2) *Physical Phases.*
        - (3) *Morphological Phases.*
2. MOTO-SENSORY ACTIVITIES OF LIFE.
    - *a.* MOTION: CONTRACTILITY.
    - *b.* SENSIBILITY: IRRITABILITY.
3. REPRODUCTION.

THE PHYSIOLOGY OF THE CELL: CYTOLOGY.

A. LIVING SUBSTANCE: PROTOPLASM.

1. THE PHYSICAL PROPERTIES OF PROTOPLASM.

ONE'S knowledge of a substance is gained through the senses. The most far-reaching sense—vision—is the one usually appealed to first, and one naturally determines first of all whether the substance is solid or fluid, whether it is transparent or opaque. Through other senses one determines whether the substance is heavy or light, etc.

Protoplasm exists only in minute portions, so mixed with the substances which it has formed that it is visible only through the aid of a microscope. That instrument reveals protoplasm as a viscous fluid. The consistency is more fluid in the active protoplasm of a growing plant or animal than in the dormant protoplasm of a seed. Whether protoplasm is thin viscous or thick viscous in consistency depends upon the amount of water which it imbibes. Seeds sometimes become very dry. When placed in the ground they cannot germinate,—the protoplasm cannot pass from its dormant condition to an active one,—until it first absorbs water; a portion of which is absorbed by the protoplasm and a portion by the stored nutriment of the seed.

In thin layers or threads protoplasm is gray and translucent. In thick threads or globules immersed in water it seems to be somewhat more strongly refractive than the water.

When a minute organism or cell, consisting of a drop of protoplasm enclosed in a delicate membrane, is studied in distilled water, it will be observed to swell up, almost bursting the enclosing membrane, but there is no evidence that any of the protoplasm passed through the membrane. If one immerses the organism in a five per cent. salt solution, it will shrivel, indicating that something has passed out of the membrane, but there is no evidence that any of the protoplasm has passed through the membrane. Protoplasm imbibes water, but it is not diffusible.

Incidental to the observations just described, it would be noticed that the protoplasmic organism sinks to the bottom of the distilled water, and rises to the top of the strong salt solution,—it is heavier than distilled water, and it is lighter than the salt solution. Protoplasm has a specific gravity greater than 1. If one were to increase the specific gravity of the surrounding liquid until the protoplasmic body would just float, neither rising nor falling, he would have only to determine the specific gravity of the liquid to know that of the protoplasm. In this way Jensen, in 1893, found the specific gravity of a paramœcium to be 1.25. Living organisms may change their specific gravity through the absorption and deposit of heavy mineral substances such as $CaCO_3$ or SiO_2, or through the formation and retention of such substances as carbonic acid gas or fat.

2. THE CHEMICAL PROPERTIES OF PROTOPLASM.

As Nature's unaided vision reveals nothing of the physical properties of protoplasm, so does her unaided taste and smell reveal nothing of the chemical properties of protoplasm. We bring to the aid of these primitive chemical tests refined process of analysis, through the aid of which one gains a knowledge of the elements which combine to form protoplasm. Pure protoplasm has not been analyzed, because it cannot be gotten in sufficient quantity.

There are reasons for believing that pure protoplasm does not differ much from albumin in composition. Egg albumin must contain all of the elements found in protoplasm, because the protoplasm of the chick is built up from the albumin of the egg. Albumin consists of carbon, hydrogen, nitrogen, oxygen, and sulphur, with certain mineral salts, associated in loose chemical combination—salts which represent phosphorus, chlorine, sodium, potassium, calcium, iron, and magnesium. The analysis of the bodies of animal and plant organisms reveals the universal presence in these bodies of the following elements : C, H, N, O, S, P, Cl, Na, K, Ca, Mg, and Fe. Rarely one or more of the following elements is found : Si, Li, Fl, I, Br, Al, Mn.

Just why living matter should be constructed from the elements named, rather than from such elements as lithium, berylium, boron, titanium, chromium, zinc, lead, etc., has been the subject of some controversy. Verworn (" Allgemeine Physiologie,"s. 106) calls attention to the fact that the elements of which living matter is composed are elements of light atomic weight. The following table may throw some light upon the question :—

TABLE SHOWING THE RELATION OF ATOMIC WEIGHT AND DISTRIBUTION TO SELECTION BY LIVING ORGANISMS.

ELEMENTS in order of importance to life.	O, H, C, N, S, P, Cl, Na, K, Ca, Fe, Mg,——Si, Li, Fl, I, Br, Al, Mn.
In order of atomic weight. Line *a*, found in life; *b*, sometimes found; *c*, never found in life.	*a.* H=1, C=12, N=14, O=16, Na=23, Mg=24, P=31, S=32, Cl=35.5, K=39, Ca=40, Fe=56. *b.* Li=7 . . . . Fl=19 . . Al=27, Si=28. . . . . Mn=55 . . . . Br=80 . . . . . I=127. *c.* Be=9.4, Bo=11, Ti=48, V=51, Cr=52.5, Ni=58.5, Co=59, Au=63, Zn=65, Ga=69, As=75, Se=79, Rb=85, Sr=87.5, Zr=90, Ni=94, Mo=96, Ru, Ag, Sn, Ro, Cd, Pd, In, and about 25 more elements.
In order of distribution on the earth's surface.	O, H, C, N, Ca, Fe, Cl, Na, K, Li, Mg, Si, S, P, Al, I, Br, Fl, Mn, etc.

The facts above tabulated justify one in making two generalizations: (I) The elements which enter into the composition of living substance are, in general, those of lightest atomic weight. (II) The elements which enter into the composition of living substance are, without exception, abundant elements of wide—practically universal—distribution.

The chemical compounds which are found in living matter may be divided into organic and inorganic. The organic compounds may be classified as proteids, fats, and carbohydrates. The proteids are very similar to living protoplasm in composition. As an example of proteids, one may take pure egg albumin, whose formula, according to Hofmeister, is $C_{204}H_{322}N_{52}O_{66}S_2$. All proteids contain C, H, N, O, and either S or P. The nucleo-proteids concontain phosphorus. Fats and carbohydrates are non-nitrogenous substances. The typical fat—tripalmitin—has the formula $C_3H_5(C_{16}H_{32}O_2)_3$. The typical carbohydrate—glucose—has the formula $C_6H_{12}O_6$. Note that these compounds are both formed of carbon, hydrogen, and oxygen, and that the proportion of oxygen in the fat is very much smaller than that in the carbohydrate. Some of the inorganic compounds associated with living matter are: $NaCl$, Na_2CO_3, Na_2HPO_4, $Ca_3(PO_4)_2$, $NaHCO_3$, $MgCl_2$, $KHSO_4$.

3. THE MORPHOLOGY OF LIVING SUBSTANCE.

a. The Structure of Protoplasm.

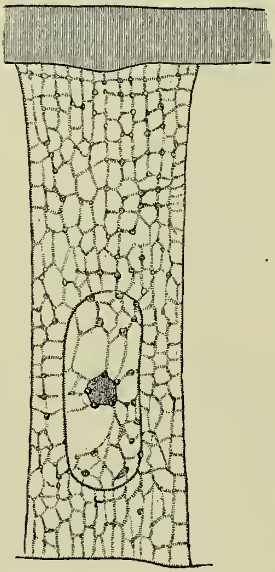
If protoplasm be studied under very high powers of the microscope it will present an appearance such as shown by Bütschli in the accompanying figures (Figs. 1*a* and 1*b*). This appearance has been differently interpreted by different observers. Bütschli and his followers contend that protoplasm is a "foam-like, alveolar structure, like an emulsion, in which the firmer portion forms the walls of separate chambers filled with the more liquid substance" (Wilson). Fleming, Van Beneden, Strasburger and others believe "that the more solid portion consists of coherent threads which extend through the ground substance," usually forming a fine meshwork or *reticulum* (Wilson). Adopting the more generally accepted second interpretation, we have protoplasm represented by two substances. (I) the more dense and refractive reticulum, thread work, or spongioplasm, and, (II) the less dense, ground substance, *cytolymph*, or hyaloplasm. Lower powers of the microscope reveal minute granules which are shown by Bütschli's figures to be located in the threads of the reticulum or spongioplasm. Some of the granules may be only apparent, and represent the confluence of several threads of spongioplasm; but some are undoubtedly actual granules of living substance.

These granules are called *microsomes*, and have been held by some investigators to be the "elementary units of structure standing between the cell and the ultimate molecules of living matter" (Wilson).

b. Structure of the Cell.

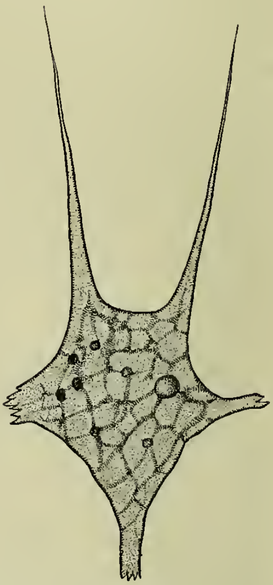
Living substance or protoplasm exists only within structures called cells. The early microscopists saw the little polyhedral, cellulose chambers of plants, and chose the word cell as most appropriate. The contents of this little chamber were collectively called protoplasm by Mohl (1846), but its importance was overlooked. Schultz, Kölliker, and others recognized finally that the protoplasm is essential, and that the cell wall is unessential; the amœba and the white blood-corpuscle, for example, having no cell wall. Schultz (1863) defined the cell as "a simple globule of protoplasm containing a nucleus." After the discovery of the centrosome by Van Beneden (1876) it became necessary to define the cell anew. In 1890 Bauer defined it as "a globule of protoplasm containing a nucleus and centrosome." But certain lower forms of life, as most bacteria, have no nucleus or centrosome. In 1895, Verworn of Jena defined the cell as "a body consisting essentially of protoplasm in its general form, including the unmodi-

FIG. 1*a*.



Epidermal cell of an earthworm (× 3000).

FIG. 1*b*.



Expanded end of a rhizopod's pseudopod (× 3000).

fied cytoplasm, and the specialized nucleus and centrosome; while, as unessential accompaniments, may be enumerated: (I) the cell membrane (II) starch grains (III) pigment granules (IV) oil globules (V) chlorophyll granules." Wilson (1896) most effectually defines the typical cell diagrammatically. (See Fig. 2.) A careful study of this diagram in connection with Graf's drawing of a nephridial cell from a leech (Fig. 3) will give the reader a clear conception of the present knowledge of the structure of the cell. The living substance of the cell is called protoplasm. That portion of the living substance which is outside of the nucleus is called *cytoplasm*, while the living matter of the nucleus is called *nucleoplasm*.

Fig. 2.

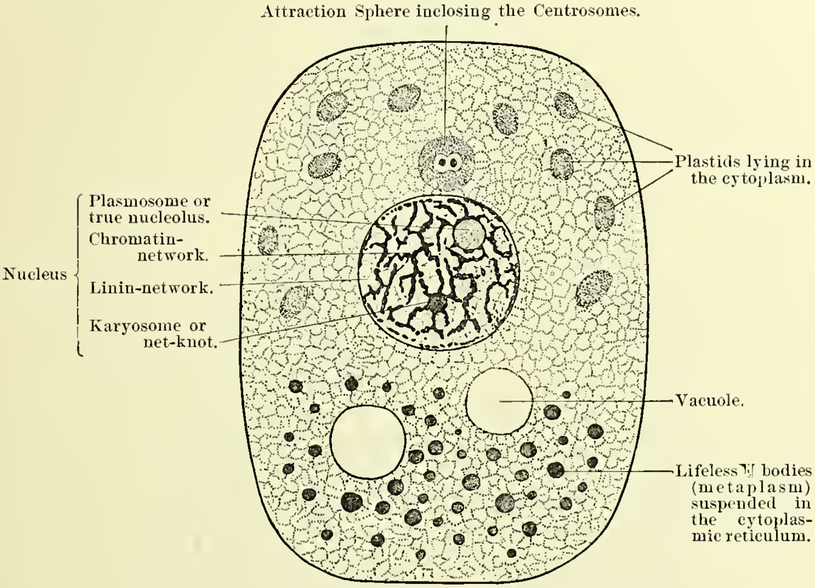
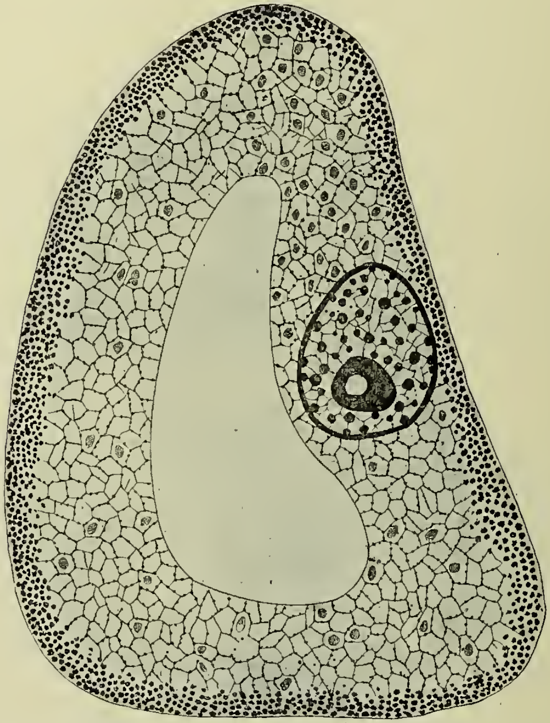

Attraction Sphere inclosing the Centrosomes.
Plastids lying in the cytoplasm.
Nucleus
Plasmosome or true nucleolus.
Chromatin-network.
Linin-network.
Karyosome or net-knot.
Vacuole.
Lifeless bodies (metaplasm) suspended in the cytoplasmic reticulum.

Diagram of a cell. (After Wilson.)

1. **Cytoplasm.**—In most unicellular organisms, and sometimes in metazoa, the cytoplasm is differentiated into the inner endoplasm and a somewhat denser exoplasm. The latter produces the cell membrane when that is present, or in its absence takes its place. Cilia are outgrowths from the exoplasm. Wilson calls attention to the fact, that "it appears to be a general rule that the nucleus is surrounded by protoplasm of relatively slight differentiation (endoplasm), while the more highly differentiated products of cell activity are laid down in the more peripheral region of the cell. The fact that the reticulum of the cytoplasm has not been

found in all cells—especially certain plant cells—leads some biologists to look upon it as an incidental, or even accidental, structure rather than a typical one. Besides the division of the cytoplasm into exoplasm and endoplasm, it may be divided into spongioplasm and cytolymph. The spongioplasm may be represented by the reticulum made up of threads of dense protoplasm in which the microsomes float, or, in the absence of a reticulum, the spongioplasm is represented only by the microsomes which float in the cytolymph. The plastids are differentiations of the cytoplasm. They are capable of growth and division. They may be looked upon as metabolic organs of the cell. They form starch grains, chlorophyll grains, or pigment corpuscles, from constituents of the cytolymph. Those that form starch grains are called

Fig. 3.



Section through a nephridial cell of the leech, *Clepsine*. (Drawn by Arnold Graf from one of his own preparations.)

The center of the cell is occupied by a large vacuole, filled with a watery liquid. The cytoplasm forms a very regular and distinct reticulum with scattered microsomes which become very large in the peripheral zone. The larger pale bodies, lying in the ground-substance, are excretory granules (*i. e.*, metaplasm). The nucleus, at the right, is surrounded by a thick chromatic membrane, is traversed by a very distinct linin-network, contains numerous scattered chromatin-granules, and a single large nucleolus within which is a vacuole. Above are two isolated nuclei showing nucleoli and chromatin-granules suspended on the linin-threads. [Wilson: *The Cell, in Development and Inheritance*, 1896.]

amyloplasts ; those that form chlorophyll are called chloroplasts, and those that form pigment grains are called chromoplasts. Inclosed within the cytoplasm, and formed from it either by the plastids, the nucleus, or otherwise, are many lifeless products of cell metabolism—starch grains, chlorophyll grains, pigment grains, oil globules, excretory granules, etc. Some of these represent reserve nutriment, and some of them, waste matter. The vacuole is a globule of food material, or of waste material in solution. It is seen only in lower forms of plant and animal life.

2. **The Nucleus: Nucleoplasm.**—"A fragment of a cell deprived of its nucleus may live for a considerable time, and manifest the power of coördinated movement without perceptible impairment. Such a mass of protoplasm is, however, devoid of the powers of assimilation, growth, and repair, and sooner or later dies. In other words, those functions that involve destructive metabolism may continue for a time in the absence of the nucleus ; those that involve constructive metabolism cease with its removal. The nucleus is generally regarded a controlling center of cell activity, and hence a primary factor in growth, development, and the transmission of specific qualities from cell to cell, and so from one generation to another" (Wilson).

(*a*) THE STRUCTURE OF THE NUCLEUS is shown, in a general way, in the diagram of the typical cell (Fig. 2). Note, in that figure : (α) The nuclear membrane ; (β) The nuclear reticulum divided into (I) the *chromatin reticulum*, and (II) the *linin reticulum;* (γ) the Nucleoli represented by (I) the true nucleolus or *plasmosome*, and (II) the net-knots or *karyosomes ;* (δ) The nuclear sap or *karyolymph* which fills the meshes of the network.

(*b*) THE CHEMISTRY OF THE NUCLEOPLASM may be briefly summarized: (α) *Chromatin* is the substance which forms the chromatin reticulum and the karyosomes. (β) *Linin* is the substance which forms the linin or achromatic network. (γ) *Paralinin* forms the karyolymph or nuclear sap. (δ) *Pyrenin* forms the plasmosomes. (ε) *Amphipyrenin* forms the substance of the nuclear membrane. It is probably identical with linin (Wilson).

3. **The Centrosome.**—This body is now generally regarded as the especial organ of cell division and in this sense as the dynamic center of the cell. The centrosome was discovered, and described by Van Beneden (1876–1883), and named by Boveri (1888). The structure of the resting centrosome is sufficiently shown in the diagram of the cell. It is shown there lying in the cytoplasm beside the nucleus,—its typical position,—though it may lie within the nuclear membrane. The function of the centrosome is so prominent a part of the process of cell division that it will be described under reproduction of the cell.

c. Form and Size of the Cell.

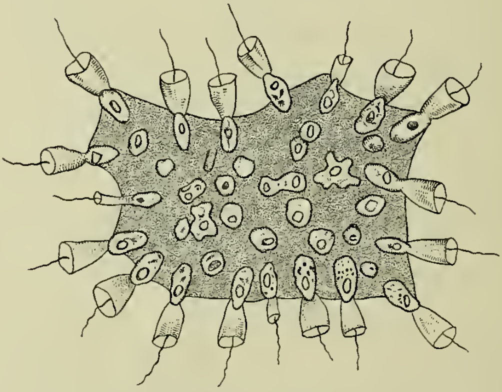
The simplest form is spherical, but many factors work together to modify this primitive form, so that one may find cells that are regularly or irregularly spherical, polyhedral, prismatic, cylindrical, discoidal, fusiform, or linear. Some cells, as the ganglion cells, may be too irregular to admit of any of these rather definite terms.

The ovarian egg of the bird or reptile is a cell, which differs from the typical cell only in having a prodigious store of fat and other food materials, thus stored for the nourishment of the developing animal. The ovarian egg of an ostrich is several centimeters in diameter. On the other hand some cells are exceedingly minute. Eberth's Typhus bacillus is about 0.9μ in diameter, *i.e.*, eleven thousand, lying side by side, would hardly reach one centimeter. The average animal cell is about 10μ in diameter.

4. THE INDIVIDUALIZATION OF LIVING SUBSTANCE.

Definition.—*An organic individual is a unified mass of living substance in a form capable of maintaining itself.* The smallest mass of living substance capable of maintaining itself is a cell. The cell is, therefore, an elementary organism; it is, at the same time, the lowest order of individual, or an individual of the first order. Ex.: Amœba Paramœcium, Stentor, Vorticella, Desmid, Yeast-cell, Protococcus, Ovum, Leucocyte. Note that, in the examples cited, all but the last two are actual, independent individuals leading a separate existence; while the ovum is a single cell capable of producing an individual capable of self-maintenance, and the leucocyte is virtually and potentially an individual, but it

Fig. 4.



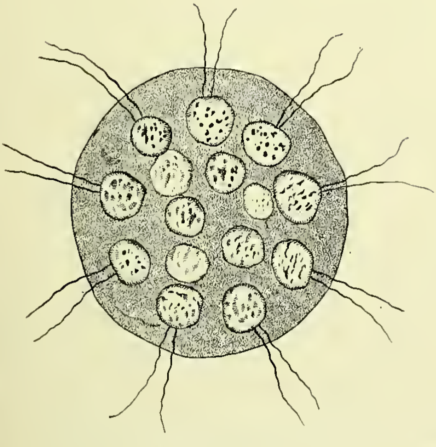
Protospongia Haeckelii, an individual of the II order.

has merged its individuality in that of the great organism of which it is a part. Thus we may find two series of examples, one representing actual, and one virtual individuals. The latter, in turn, may be subdivided into a series representing individual development (ontogenic series), and one representing stages of tissue development.

Colonies of cells, similar as to form and function, constitute individuals of the second order. Ex.: Protospongia, Eudorina, Morula or Blastula stage of development, any tissue. In the animal kingdom Protospongia Haeckelii (Fig. 4), and in the plant, Eudorina elegans (Fig. 5), we see examples of *colonization and combination for mutual help and protection.* This marks a long step in the advance of living organisms, but all of the cells are practically alike in form and function.

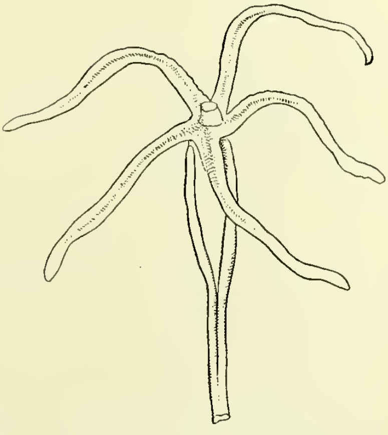
A unified mass of living substance, composed of two or more colonies of similar cells,—two or more tissues,—forms an individual of the third order. Ex.: Hydra (Fig. 6), the Thallophytes among plants, Gastrula stage of development, an organ. This marks another long step in organic evolution—*specialization of structure and function.*

FIG. 5.



Eudorina elegans, an individual of the III order.

FIG. 6.



Hydra, an individual of the III order.

Individuals of the fourth order are composed of organs, tissues, and cells arranged in systems, such as the digestive system. Ex.: Man, Tree. Men and other animals organize colonies or states which represent individuals of the fifth order. The following table gives a general view of the individualization of living substance :

	Order.	Actual Individuals. Taxonomic Series.	Virtual Individuals.	
			Ontogenic Series.	Histogenic Series.
Individualization of Living Substance.	I.	Amœba, Desmid, Paramœcium, Diatome, Vorticella, Protococcus.	Ovum, with segmentation nucleus.	Cell: Leucocyte.
	II.	Protospongia, Eudorina.	Segmentation Stages Morula. Blastula.	Tissue: Cartilage.
	III.	Hydra, Thallophyta.	Gastrula.	Organ: Stomach.
	IV.	Man, Tree.	Adult: Man.	Systems of Organs: Man.
	V.	——	Colony or State.	——
	VI.		——?——	

B. THE PHENOMENA OF LIFE.

1. NUTRITION.

The general term nutrition includes all those activities of the organism directed toward the procuring of food, digestion, absorption, the chemical changes within the tissues (metabolism), respiration, and excretion.

a. Absorption and Excretion.

1. **Absorption and Excretion of Gaseous Material.**—Every living organism ceases to live when deprived of oxygen. Oxygen exists in a gaseous form as a constituent of the atmosphere (21 per cent.); and it is dissolved in water, so that it is accessible to terrestrial and aquatic plants and animals. For multicellular organisms the law may be stated thus: Every active cell of every living organism requires oxygen for the maintenance of activity. In the whole organic kingdom the absorption of oxygen—Respiration—is associated with the excretion of carbon dioxide and water, and with the production of heat. How are we to interpret these general facts? It was formerly believed that oxygen directly oxidized the living matter in the same way that it directly oxidizes the carbon and hydrogen of a candle, this process resulting, in both cases, in the formation of carbon dioxide and water, and the production of heat. Pflüger of Bonn found by experiment, that frogs can live several hours in an atmosphere of nitrogen, and continue to produce carbon dioxide. From this and

other experiments Pflüger concluded, that "The first impulses to the chemical processes of respiration are not given by the oxygen which enters from without; but that primarily a decomposition of molecules takes place within the protoplasm, resulting in the liberation of carbon dioxide, and that hence the incoming oxygen effects a simple restitution of the integrity of the new molecules which are formed." This gradual breaking up of the highly complex protoplasm into simpler and simpler bodies which combine with oxygen, liberating the energies for the life processes, is called katabolism or destructive metabolism. The reverse process—anabolism, assimilation, or constructive metabolism—is one of the most interesting and important processes in the realm of nature. Inasmuch as katabolism, or destructive metabolism, ends with the liberation of carbon dioxide and water, with the consumption of oxygen, and the production of heat, may we not expect that the building up of living matter—anabolism, assimilation, constructive metabolism would begin with the consumption of carbon dioxide and water, and the liberation of oxygen, and that the process would require heat from some external source? This process, which one would expect, is exactly that which is actually going on in nature. Every green plant absorbs, as food, carbon dioxide and water; these are taken into the protoplasm, and, under the influence of the green plant coloring matter—chlorophyll—and of the light and heat of the sun, the carbon dioxide and water are combined to form dextrose ($C_6H_{12}O_6$). After dextrose is once formed, the protoplasm of the cells is able to appropriate it to build up protoplasm. In recapitulation we may say, then: (I) *All living cells absorb free oxygen in their respiratory process.* (II) *All living cells excrete carbon dioxide in their respiratory process.* (III) *All green plant cells absorb carbon dioxide as food.* (IV) *All green plant cells excrete oxygen as a waste product in their nutritive process.*

2. **The Absorption and Excretion of Liquid Substances.**—Most of the water used in the plant economy is absorbed in the fluid state. Much water leaves the bodies of both plants and animals in the form of gas or vapor, but a large part of this is not the product of excretion, it is the product of evaporation. All of the water used in the animal economy is absorbed in the fluid state. Moreover all inorganic matter is absorbed into cells in the form of solution in water. With few exceptions it is also true that the food of most animals, though received into the alimentary canal in the solid state, is changed to the fluid state—by solution in water—before it is absorbed by the cells which line the alimentary canal. A most interesting problem presents itself at this point—*The selective powers of living cells.* Living side by side in the sea are one-celled animals,—some species bearing silicious shells, while other species bear calcareous shells. The first

species has selected the silica from the sea water, while the second has selected the calcium carbonate. Growing side by side in the shallow sea water may be several species of the seaweed—Fucus,—but each species will have selected different but constant proportions of the mineral matter dissolved in the sea water. The following table from Pfeffer, cited by O. Hertwig, illustrates the point in question :—

ASH-CONSTITUENTS.	FUCUS VESICULOSUS.	FUCUS NODOSUS.	FUCUS SERRATUS.	LAMINARIA DIGITATA.
Potassium oxide . . . . K_2O	15.23%	10.07%	4.51%	22.40%
Sodium oxide . . . . . . Na_2O	24.54%	26.59%	31.37%	24.09%
Calcium oxide . . . . . . CaO	9.78%	12.80%	16.36%	11.86%
Silica . . . . SiO_2	1.35%	1.20%	0.43%	1.56%

In the bodies of higher animals each cell is bathed in blood, or lymph, containing many food materials in solution, but the bone cells select the $CaCO_3$ and $Ca_3(PO_4)_2$, while the muscle cells select from the nutrient fluid proteids with various salts; and so on, every cell selecting the needed food, and rejecting what is not needed.

3. **The Absorption of Solid Bodies.**—Can living cells absorb and appropriate as food solid bodies? This can only be accomplished by cells devoid of a cell membrane, or cells having holes in the membrane. As most cells are enclosed in a membrane, it is clear that the absorption of solid bodies is limited to naked animal cells, *i. e.*, to the Rhizopoda and Ciliata among lower animals, and to leucocytes, and possibly ciliated epithelium, among higher animals. The ability to absorb particles is of very great importance to the higher animals, and is utilized under the following circumstances: (I) During embryonic development in absorbing useless parts. (II) During life in disposing of solid impurities, broken-down, red-blood corpuscles, etc. (III) During infectious disease the leucocytes constitute a bodyguard in opposing the spread of microbes in the blood and tissues by simply absorbing and digesting them. Metchnikoff says: "Between micro-organisms and leucocytes an active war is raging. This is settled in favor of one or the other party, resulting in the death or the recovery of the affected animal."

b. Metabolism.

The term *metabolism* is used to designate the chemical changes to which matter is subjected under the influence of life. When the chemical change combines simpler into more complex substances, the term *anabolism*, or *constructive metabolism*, is used; while for the reverse process *katabolism*, or *destructive metabolism*. is used.

1. **Chemical Phases.**—It has already been stated that under the influence of chlorophyll and sunlight the plant cell is able to cause a combination of carbon dioxide and water to form dextrose, and that the cell protoplasm has the power of replenishing its substance from the dextrose; further, that through successive combinations with oxygen the protoplasm is, step by step, reduced to simpler compounds, until it is finally expelled from the organism in the form of carbon dioxide and water. This is, in fact, about all that is known with absolute certainty. It was formerly believed that the combination of carbon dioxide and water was direct, and as follows: $6CO_2+6H_2O=C_6H_{12}O_6+6O_2$; but it is now believed that the combination is indirect, and somewhat as follows: $CO_2+H_2O=O_2+CH_2O$ (Formic Aldehyde) and $6CH_2O=C_6H_{12}O_6$ (Dextrose). It has been convenient to describe the two extreme steps of the process of metabolism, first the combination of the inorganic elements of our environment—CO_2 and H_2O—within a green plant cell, under the influence of the energy of the sunlight, to form dextrose, and finally the katabolism, or destructive metabolism, of the animal cell into the same inorganic elements. Between these two extremes are many intermediate steps. In the plant kingdom the steps are ascending ones, for the protoplasm of the plant cell is able to make a long list of carbohydrates, then of fats and oils, then of proteids, and finally, to replenish its own substance, or to make protoplasm. The slight activities of the plant require katabolism of living substance for the liberation of the needed energy, but, on the whole, anabolism, or constructive metabolism, predominates, and the plant kingdom bequeaths to the animal kingdom a rich legacy of starch, cellulose, sugar and other carbohydrates, of oils and of proteids. Animals, on the other hand, are unable to appropriate either the free inorganic elements or the free sun-energy of their environment; they depend directly or indirectly upon plants or plant products. The active life of animals involves the dissipation of much energy. This energy is liberated by the katabolism of living substance; so, in the animal kingdom, katabolism, or destructive metabolism, predominates.

The following figure illustrates the relation of anabolism and katabolism,—of constructive and destructive metabolism in the plant and animal kingdom. (See Fig. 7.)

In the successive metabolic changes ferments play a very important part. A ferment is a proteid body, capable of causing a chemical change without itself being consumed or essentially altered. It is clear from this definition that a very small amount of ferment is able to accomplish a very large amount of work. Examples: Diastase, Ptyalin, Pepsin, etc., etc.

Fig. 7.

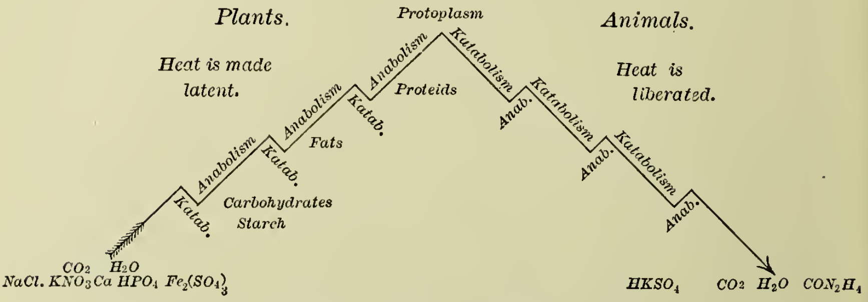


Diagram illustrating the relation of plants and animals to anabolism and katabolism.

2. **Physical Phases.**—Incidental reference has already been made to the liberation of energy and to the making latent of energy. As stated in the introduction, the law of the conservation of energy applies to animal bodies as it does to a steam engine.

(*a*) Forms of Energy.—(i) Atomic Attraction or Chemical Energy, (ii) Molecular Attraction or Cohesion, (iii) Molar Attraction or Gravitation, (iv) Heat, (v) Light, (vi) Electricity, (vii) Magnetism, (viii) Mechanical Energy, Pressure, Tension.

(*b*) The Cell's Source of Energy (*α*) *Chemical Energy.*—*The combination of atoms into molecules leads to a liberation of energy while the separation of a molecule into its atomic elements requires energy.* For example, the combination of hydrogen and oxygen into water liberates heat; while the decomposition of water into its constituents requires the expenditure of energy. But in the usual chemical reaction there is both a separation and a combination of the atoms.

This leads to the formulation of the following law: *If, in a chemical reaction, stronger affinities are satisfied than broken, energy will be liberated; if, on the other hand, stronger affinities are broken than satisfied, energy will be required to bring about the reaction.* Examples:

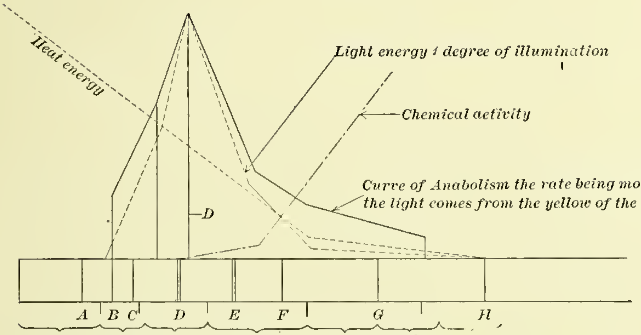
(i.) $C_3H_5(C_{17}H_{35}COO-)_3 + 163O = 55H_2O + 57CO_2 + \text{Energy}$

(ii.) $6CO + 6H_2O + \text{Energy} = C_6H_{12}O_6 + 6O_2$.

Potential chemical energy is the common source from which spring all the other forms of energy involved in the phenomena of life.

(*β*) *Energy of Heat and Light.*—The source of this form of energy for the realm of living nature is sunlight, and, as previously stated, it makes its entrance into this realm through the chlorophyll-bearing plant-cell. Moreover, not all of the energy of sunlight is thus utilized, the cell selects energy as it does matter. Pfeffer's observations have led to the following figure. (See Fig. 8.) As to the action of the warmth of the sun's rays upon animal metabolism, it is rather indirect than direct, as it simply economizes animal heat and so decreases katabolism or destructive metabolism. The same may be said of such artificial measures as shelter, clothing and heating,—they all economize animal heat, thus decreasing katabolism.

FIG. 8.



Pfeffer's diagram showing the relation of light to assimilation in chlorophyll-bearing plants.

(*c*) THE CELL'S MANIFESTED ENERGY.—This appears in the form of cell-motion, of heat, and in certain organisms in the form of light or of electricity.

2. MOTO-SENSORY ACTIVITIES OF LIFE.

Let us, for a moment, recall Spencer's definition of Life: "Life is the continuous adjustment of internal relations to external relations." The same idea may be stated in slightly different terms: *Life* in an *organism* is a *correlation* of *energies, manifested* by a *continuous adjustment* of its *internal activities* to its *environment.* All the activities of an individual may be divided into two classes: 1st. *Egoistic Activities*—which contribute to self-preservation; Egoism; Individualism: 2d. *Phyletic Activities*—which contribute to the preservation of the race; Phyleticism; Altruism. In the first case we find the organism in a struggle for life—life of self; in the second case we see the organism sacrificing self for the preservation of the species. Applied more specifically to physiology, the first class of activities are those which contribute to the *procuring* of *nutriment,* to *self-defence* against danger, and, in higher animals to the *pursuit* of *pleasure;* while the second class is represented by reproduction, protection of offspring, etc., and in higher animals philanthropy. Self-defence as well as the procuring of food usually involves *motion;* frequently also locomotion, on the part of the organism. Motion is always in response to a stimulus; but response to a stimulus involves irritability. It must be evident, then, that the activities of the moto-sensory organs and tissues are inter-dependent and that they must follow a particular sequence. Let us turn our attention first to motion and contractility.

a. Motion and Contractility.

For the most part the motion of living organisms is due to their possession of the property of contractility, but there are among the plants various other methods of moving the parts of the individual, or even of moving the whole individual (locomotion), than through contractility of living substance. It would seem as if Nature had tried various experiments and had finally in the higher animals specialized the property of contractility as the most efficient method of producing motion.

1. **Motion Without Contractility.**—(*a*) MOTION THROUGH SWELLING OF THE CELL WALL.—The spores of the common horse-tail rush, *Equisetum,* are provided with four little cellulose appendages (elaters) which wrap tightly around the body of the spore when moist and extend when dry. The alternation of these two conditions, accompanied by an alternation of flexion and extension, causes the little spore to move slowly over the surface of the soil, to some distance from the parent plant.

(*b*) MOTION THROUGH CHANGE OF CELL TURGOR.—The closing of leaves at night and their opening in the sunlight is a phenomenon known to every school child. How do the leaflets of the clover, oxalis, or sensitive plant close together? In the axil of every leaf is a motile organ composed of thick-walled parenchyma cells between the fibro-vascular bundle and the epidermis below, while the fibro-vascular bundle, though flexible, is not extensible. The tissues above the fibro-vascular bundle are very scantily represented. When the parenchyma cells above mentioned become turgid with water, the leaf-stalk is erected; if the water is suddenly allowed to escape from the cells the leaf falls to the nocturnal or sleeping position by its own weight. When the proper stimulus comes, the protoplasm imbibes water again and the leaf is erected.

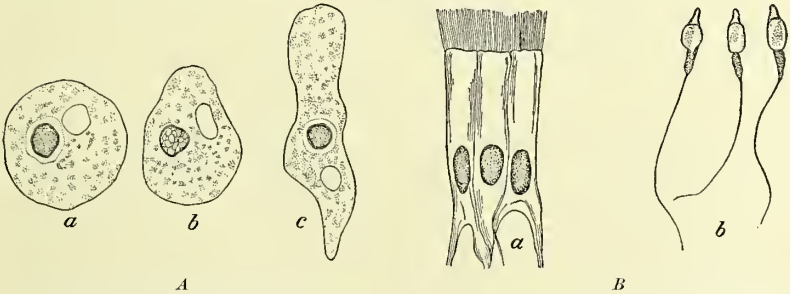
(*c*) MOTION THROUGH CHANGE OF SPECIFIC GRAVITY.—Certain marine animals of low rank (Radiolaria, Siphonophora) utilize their own excretions to buoy them up. By retaining their carbon dioxide it so decreases their specific gravity that they rise to the top of the water. On the other hand, by giving off the carbon dioxide, or by deposit of calcium salts or of silica within their tissues they will again sink.

(*d*) Motion through Secretion.—The movements of desmids and diatoms were, for a long time, a subject of study. It finally became apparent that the minute organism was leaving behind it a little trail of secreted mucus, which served the double purpose of anchoring it to its place and of pushing it along.

(*e*) Motion through Growth-tension.—The seedpod of the touch-me-not grows in such a way that the opposite segments exert a nicely-balanced tension against each other. If the ripe pod be gently pressed the equilibrium is destroyed and the pod flies to pieces, throwing the seeds out.

2. **Motion Through Contractility.**—(*a*) Amœboid Motion.—The amœba when in a state of rest is spherical, and presents to the medium in which it floats the minimum surface. Its motion consists in the pushing out of a portion of its periphery. (See Fig. 9.) This act increases the surface exposed to the medium and thus increases the opportunity for the exchange of oxygen and carbon dioxide. It also increases the opportunity to get food. The hungry amœba is always active. The extensions of its protoplasm—its pseudopodia—may be numerous, and they vary from minute to minute. This form of motion is observed also in the white blood-corpuscles or leucocytes.

Fig. 9.

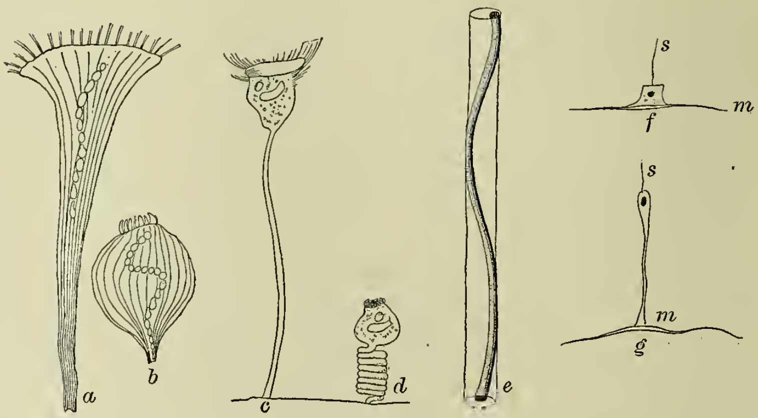


An amœba in different phases of motion (*A b c*). Ciliated epithelial cells (*B a*). Spermatozoa with motile flagella (*B b*).

(*b*) Ciliary Motion.—Many cells are provided with fine protoplasmic extensions, which are permanent and may cover the whole surface of the cell, or a limited surface, and may be numerous or few. In active cells the cilia are in a state of constant motion, which consists in a quick whip-like motion in one direction, followed by a slow return. All of the cilia on the end of a ciliated cell of the human respiratory tract (Fig. 9, *B a*) move in the same direction at the same time. Furthermore, all of the cilia of all the cells in any region act in unison, an undulatory motion running over the whole surface. The result of such a movement of the cilia is to carry over the surface any small particles or accumulations of secretions. Cilia are capable of a prodigious amount of work. The ciliated epithelium of a frog's œsophagus will carry a 75-mgm. lead weight up a 60-degree incline when the lead presents as much as 20 square millimeters. One form of ciliary motion is that presented by the spermatozoa. (Fig. 9, *B b*.) Here the one cilium, or flagellum, possesses a scull-like motion, which propels the spermatozoön through liquids or over moist surfaces.

(*c*) Muscular Motion, or Motion by Fibrillary Contractility.—A third form of motion is that through contraction of fibrillæ. Contractile fibers appear very low in the animal scale. The *Stentor*,—Protozoa, Ciliata,—(See Fig. 10, *a*, *b*), possesses numerous fine fibrillæ in the exoplasm of the cell. Through the contraction of these fibrillæ the body may retract upon the little foot until it assumes a nearly spherical form. The closely related Vorticella has a long slim pedicel to its bell-shaped body. The stalk has the property of retracting into a closely coiled spiral, a striking view under the microscope. Figure 10, *c*, *d*, *e*, shows the mechanism which produces this remarkable effect. There is a single contractile fibril passing spirally down the inside of the sheath of the pedicel. Contraction of this fibril tends to straighten it, throwing the pedicel into a spiral. Next in the progressive series the neuro-

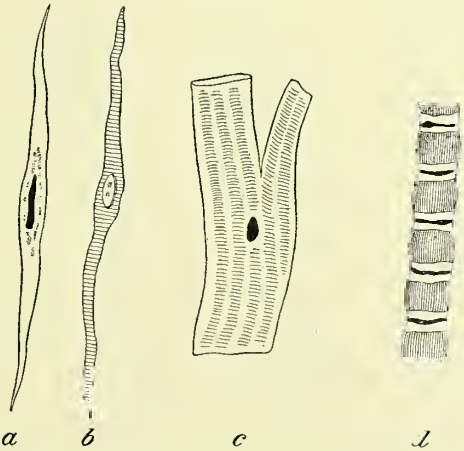
Fig. 10.



Illustrating fibrillary contractility: *a*. *Stentor* open, *b*. *Stentor* contracted. *c*. *Vorticella* open, and (*d*) contracted, with (*e*) section of pedicel of same. *f* and *g* Neuro-muscle cells of a cœlenterate. Note that the nucleated body of these cells possesses a sensitive, tactile flagellum (*s*), and a contractile fibrilla (*m*). The second one of these cells (*g*) is especially interesting because the thread of protoplasm between the body of the cell and the motor fibrilla is the functional equivalent of a motor or efferent nerve.

muscular cell of the medusa may be named. (See Fig. 10, *f*, *g*.) Muscular tissue is fairly well developed in Vermes, and very highly developed in the higher Arthropoda, especially the insecta. Figure 11, *a*, *b*, *c*, shows some forms of muscle fibers or cells from vertebrate animals. Figure 11, *d*, shows a portion of a fibrilla from a muscle fiber of an insect's wing. For a further description of the muscle-tissue of the higher animals see the anatomical introduction to the next chapter.

Fig. 11.



a. Non-striated muscle cell. *b*. Striated muscle cell of frog's heart. *c*. Striated muscle cell of mammal's heart. *d*. Striated muscle cell of insect's wing.

Muscle tissue is sensitive to various stimuli applied either directly to the muscle or indirectly to the nerve which supplies the muscle. When stimulated, the muscle responds by making a contraction which consists in a decrease in length with increase of the thickness, the volume remaining the same. Other important changes take place in a muscle-cell incident to its contraction, viz.: The chemical changes which liberate the mechanical energy of motion, also a certain amount of heat energy. These changes will be discussed at length in the chapter on the physiology of contractile and irritable tissues.

b. **Sensibility: Irritability.**

The most noticeable fact observable in the Vorticella is its motion. After observing this motion for a time, one asks: Why does it move? If the microscope slide upon which it is resting be jarred, or if it be touched by some foreign body, the contraction will take place. Evidently the organism as a whole, or some specialized portion of it, is sensitive to these mechanical stimuli.

When the amœba, resting quietly on the slide, suddenly thrusts out a pseudopodium the immediate cause is not so evident. The cause is internal. The amœba is hungry, and like all hungry organisms, it starts upon a foraging tour. In every case motion, indeed all cell activity, is in response to stimuli. The ability to respond to stimuli is called irritability. This is the characteristic of living matter, by which it is susceptible to changes in its environment; it is the primary distinguishing feature of living matter. Without it the living organism, being unconscious of changes in its environment, could originate no activity which would bring it into harmony with its surroundings, and its destruction through hunger or accident would inevitably soon follow. A complete, successful, adaptative action then requires: 1st, *Irritability;* 2d, *Motion and coördination in space and time.*

Some stimuli are external to the organism and apparent to the observer; others are internal and not apparent. The invisible stimuli are just as real as the visible ones. The internal stimulus, which starts the amœba in quest of food, is probably a chemical one.

(1) **Stimuli Classified.**—The following forms of energy act as stimuli for most cells: (I) Heat, (II) Light, (III) Electricity, (IV) Mechanical Stimuli, (V) Chemical Stimuli.

(2) **Action of Stimuli.**—(*a*) *The same stimulus may produce quite different effects in different organisms.* (Ex. ± Heliotropism, ± Chemotropism, ± Galvanotropism.)

(*b*) *Quite different stimuli will produce the same effect* in the *same protoplasmic body,* IF the sensitive body is highly specialized, *e. g.,* a muscle-cell responds to all stimuli by contracting, a gland-cell by secreting, while the stimulation of the optic nerve can only produce the sensation of light.

(*c*) *However localized the application of the stimulus, the effect is always transmitted to more or less remote parts of the organism;* therefore, we must infer the *conductivity* of living matter.

(*d*) *Stimuli are more rapidly transmitted in animal than in plant bodies.* [Human nerves, 34 ft. per second. Plant tendril 1 ft. in several minutes.]

(*e*) *The action of stimuli is more or less transient, i. e.,* the stimulated organism returns after a short period, more or less completely, to its former state of rest.

(*f*) Over-stimulation always leads to *exhaustion,* recognized at the point where even a strong stimulus fails to elicit a response.

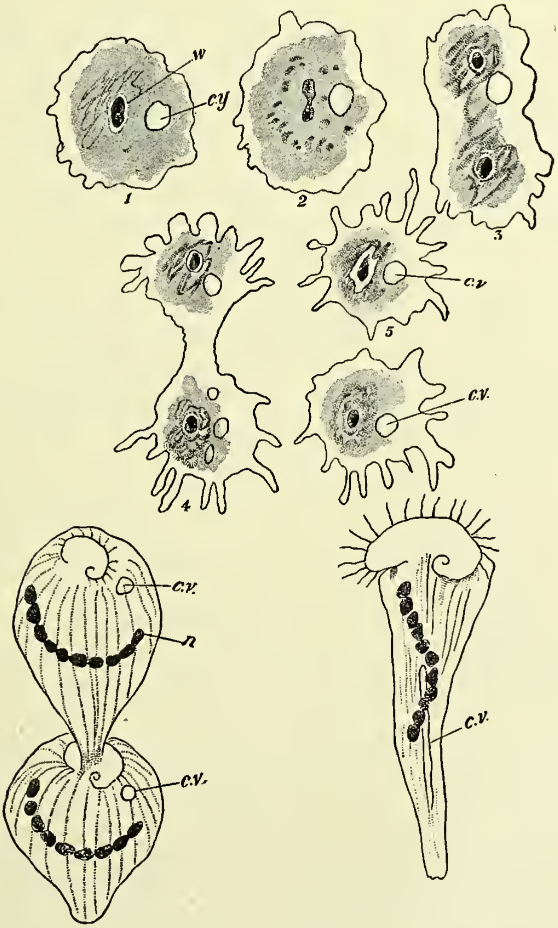
e. Reproduction.

Reproduction has already been mentioned as one of the phyletic or altruistic functions for the reason that it invariably involves on the part of the individual sacrifice of self for species.

In a general way the lower animals undergo a greater self-sacrifice in the *reproduction* of offspring while the higher animals undergo a greater self-sacrifice in the *support* and *protection* of offspring. Let us proceed to the description of the phenomena of cell reproduction.

1. **Cell-Reproduction.**—It was demonstrated by Virchow that every cell is from a cell—" *Omnis cellula e cellula.*"

FIG. 12.



Direct or Amitotic cell-division. 1–5 Division of the *Amœba*. The lower figures illustrate the division of the *Stentor*. *n*. nucleus ; *cv*. Contractile vacuole.

" No spontaneous generation of cells occurs either in plants or in animals. The many millions of cells of which the body of man is composed have been produced by the repeated division of *one* cell—the *ovum*, in which the life of every animal commences." —Hertwig.

There are two methods of cell-reproduction—*direct* and *indirect.*

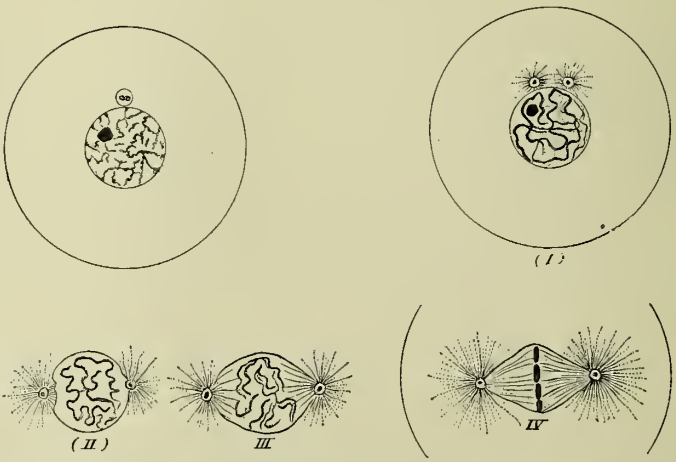
(*a*) IN THE DIRECT OR AMITOTIC METHOD the division of the cell protoplasm usually begins in the nucleus followed by the cytoplasm. The contractile vacuole usually takes part in the division. (See Fig. 12.) This form of cell-reproduction may be observed "in glandular epithelia, in the cells of transitory embryonic envelopes, and in tumors and other pathological formations."—Wilson.

(*b*) THE INDIRECT: MITOSIS OR KARYOKINESIS.—In this method the nucleus plays the principal rôle, the chromatin presenting a series of striking appearances, called the karyokinetic figures. This form of cell-reproduction is now held to be typical for nearly all healthy nucleated cells.

Karyokinesis, mitosis, or indirect cell division, presents a very long series of changes sufficiently different one from another to lead to the description of twelve to fifteen different stages. O. Hertwig and Wilson use four principal phases, one phase frequently representing several stages.

Following these authors mitosis may be thus briefly summarized: In its resting condition, which immediately precedes mitosis, one may observe a walled nucleus, with granular chromatin and a more or less clearly defined centrosome, which may have previously divided, but which is dormant.

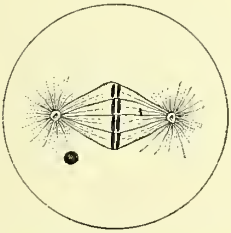
FIG. 13.



Prophases of Karyokinesis. *I, Division and migration* of centrosome; *II,* Resolution of chromatin into well-defined *thread; III,* Segmentation of same into *chromosomes; IV,* development of *amphiasters;* chromosomes equatorial. (WILSON.)

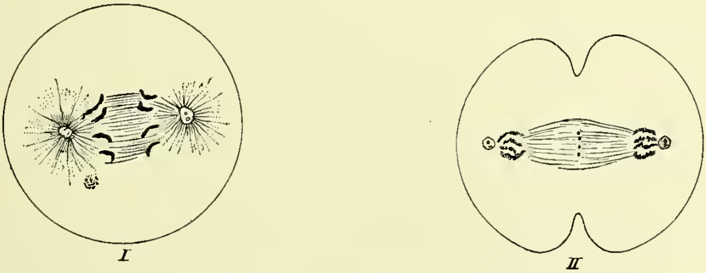
(*a*) *The Prophases* or preparatory stages. (Fig. 13.) (1) *Division* of the *centrosome* and *migration* of each young centrosome, along the circumference of the nucleus to an opposite pole of the nucleus. (II) Resolution of the chromatin substance of the nucleus into a well-defined thread or spirem, which is coiled within the nucleus. (III) Segmentation of the spirem into a definite number of *chromosomes.* "Every species of plant or animal has a fixed and characteristic number (8 to 36, 16 in man) of chromosomes which regularly recurs in the division of all of its cells. In all forms arising by sexual reproduction the number of chromosomes is even." (Wilson.) (IV) Development of the *Amphiaster* which consists of two polar *asters,* in the center of each of which lies a centrosome, also the *spindle.* The aster lies in the cytoplasm, while the spindle, formed of numerous meridional fibrillæ, formed from the achromatic network, occupies the nucleus, whose walls have in the meantime disintegrated and disappeared. (V) The chromosomes assume a position in the equatorial plane of the spindle forming the *equatorial plate.*

FIG. 14.



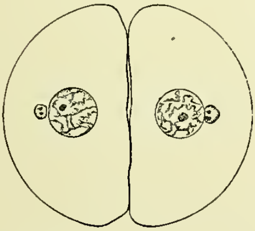
Metaphase of Karyokinesis. (WILSON.)

FIG. 15.



Anaphases of Karyokinesis. (WILSON.)

FIG. 16.



Telophase of Karyokinesis. (WILSON.)

(β) *Metaphase.* (Fig. 14.) Longitudinal division of each chromosome. "The daughter nuclei receive precisely equivalent portions of chromatin from the mother nucleus." (Wilson.)

(γ) *Anaphases.* (Fig. 15.) (I) Divergence of the two sets of daughter chromosomes toward the poles of the spindle. Probably drawn by the meridional fibers of the spindle, which seem to be attached to them. (II) The divergence of the daughter asters reveals an inner spindle, this first visible at the equator of the nucleus, and called the interzonal fibers. (III) Division of the centrosome preparatory to the next mitosis.

(δ) *Telophases.* (Fig. 16.) "The entire cell divides in two in a plane passing through the equator of the spindle, each of the daughter-cells receiving a group of chromosomes, half of the spindle and one of the asters with its centrosome." (Wilson.) (II) The chromatin becomes distributed in granular form, as found at the beginning. (III) The nucleus provides itself with another nuclear membrane.

CHAPTER II.

THE PHYSIOLOGY OF CONTRACTILE AND IRRITABLE TISSUES. INTRODUCTION.

A. PHYSICAL INTRODUCTION.

1. ELEMENTS AND BATTERIES.
2. KEYS AND ELECTRODES.
3. METHODS OF MODIFYING THE CURRENT.
4. THE INDUCTORIUM.
5. THE MEASUREMENT OF ELECTRICITY.
6. METHODS OF RECORDING RESULTS.

B. ANATOMICAL INTRODUCTION.

1. THE STRUCTURE OF MUSCLE.
2. THE STRUCTURE OF NERVES.
3. THE MUSCLE-NERVE PREPARATION.

THE PHYSIOLOGY OF CONTRACTILE AND IRRITABLE TISSUES.

A. THE MUSCLE-NERVE PREPARATION.

1. STIMULI.
2. CHANGES WHICH TAKE PLACE IN A MUSCLE IN RESPONSE TO STIMULI.
    - *a.* Change in Form.
        - (1) *Change in Length.*
        - (2) *Change in the Transverse Dimensions.*
        - (3) *The Work Done by a Contracting Muscle.*
    - *b.* Chemical Changes which take Place in a Contracting Muscle.
    - *c.* Thermal Changes which take Place in a Contracting Muscle.
    - *d.* Electrical Changes which take Place in a Contracting Muscle.
3. THE RELATION OF THE NERVE TO VARIOUS STIMULI.
    - *a.* Properties of Nerve Trunks.
    - *b.* Conductivity.
    - *c.* Irritability.
    - *d.* Pflüger's Law of Contraction.
    - *e.* The Application of the Laws of Electrotonus.

B. THE GENERAL STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM.

- (1) *The Neuron.*
- (2) *Features of the Spinal Cord.*
- (3) *Reflex Action.*
- (4) *Nerve Centers.*

II. THE PHYSIOLOGY OF CONTRACTILE AND IRRITABLE TISSUES.

INTRODUCTION.

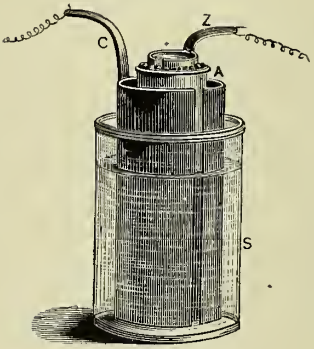
A. PHYSICAL INTRODUCTION.

INCIDENT to the investigation of the properties of muscles and of nerves, various stimuli are employed. The stimulus most used is electricity. It is taken for granted that the student has made himself acquainted with the general principles of electricity before beginning the study of physiology. The electrical appliances used in the physiological laboratory being somewhat specialized, require a brief description.

1. ELEMENTS AND BATTERIES.

The Daniell element or cell is used most in the physiological laboratory. Fig. 17 shows such a cell to be composed of four parts: The outer glass receptacle usually of one or two quarts capacity; the copper plate, a thin sheet of copper; the porous cup, of unglazed earthenware, and the zinc plate, which stands in the porous cup. The Daniell cell is a two-fluid cell: Outside of the porous cup, and surrounding the copper plate, there is a saturated solution of copper sulphate; inside of the cup, surrounding the zinc plate, there is 10 per cent. sulphuric acid. The zinc plate must have its surface amalgamated to prevent its too rapid consumption and the evolution of hydrogen gas. The zinc plate is the positive plate, while the copper plate is the negative one. Upon each plate there is a binding-screw, through which the wires may be fixed to the plates. The distal ends of the wires are called the poles or electrodes. The electrode, which is attached to the negative (copper) plate is the positive electrode or *anode*, while the electrode, which is attached to the positive plate, is the negative electrode or *kathode*. No chemical action takes place in the cell until the electrodes are brought into contact with each other when zinc is consumed with the formation of zinc sulphate and the liberation of nascent hy-

FIG. 17.

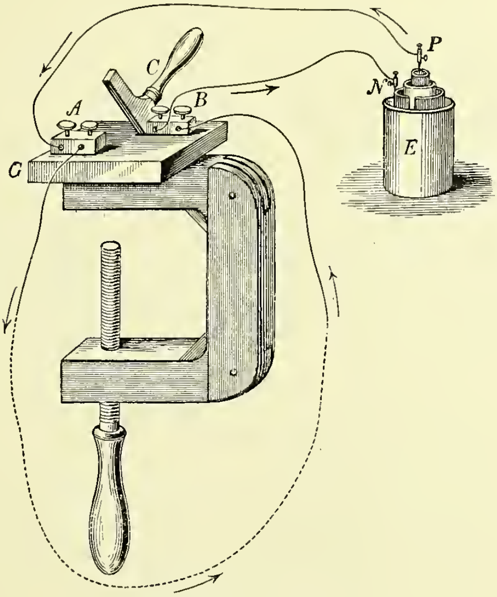


The Daniell cell.

drogen; the latter displaces from the copper sulphate copper, which is deposited upon the copper plate.

The amount of electrical energy liberated by one cell is frequently insufficient to meet the requirements of a physiological experiment. In such a case recourse is had to the multiplication of cells to form a *battery*. The high resistance of animal tissues to the passage of an electrical current makes it necessary to adopt a particular method of joining up the eells of the battery; *i. e.*, the cells are joined up *in series* or *tandem*.

Fig. 18.



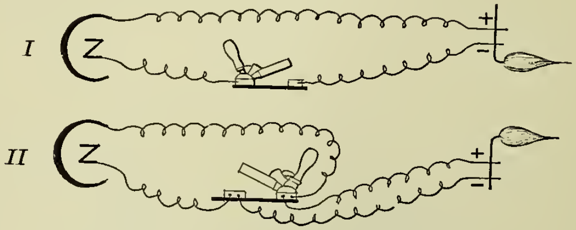
The DuBois-Reymond key.

2. KEYS AND ELECTRODES.

The key most used in physiological experimentation is the Du Bois-Reymond key (see Fig. 18). This key has the advantage of permitting two distinct uses: (I) as a simple contact key, (II) as a short-circuiting key. It is evident in the second case that when the key is closed the circuit is "short-circuited," and the current passes from the positive to the negative side through the key. When the key is opened as shown in Fig. 19, *II*, the current is thrown into the longer circuit and must traverse the nerve which lies upon the electrodes. This is the usual method of using the DuBois-Reymond key, especially with induced currents.

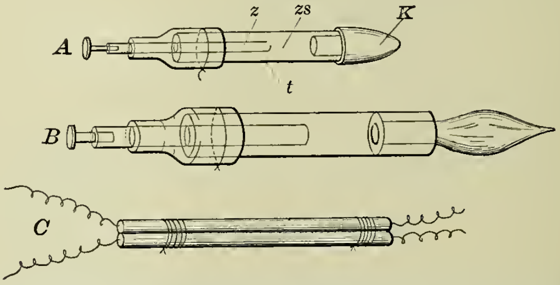
When a constant current passes from metallic electrodes into animal tissue there is a decomposition of the tissue fluids and a gradual polarization of the electrodes which disturbs the results of the experiment. To avoid this various non-polarizable electrodes have been devised (see Fig. 20). The non-polarizable electrode shown in Fig. 20, *A*, consists of a glass tube (*t*) into which an amalgamated zinc rod (*z*) extends, immersed in a saturated solution of zinc sulphate (*zs*). The zinc rod is held in position by a piece of rubber tubing, and has a binding screw at the outer end. The end of the glass tube opposite to the zinc rod is provided with a pencil of kaolin paste (kaolin powder with NaCl 0.6 per cent.). In Fleischl's electrode (*B*) a brush is used instead of the kaolin pencil. The hand electrodes (*C*) consist simply of platinum or copper wires insulated with glass or rubber.

FIG. 19.



Showing uses of the DuBois-Reymond key.

FIG. 20.



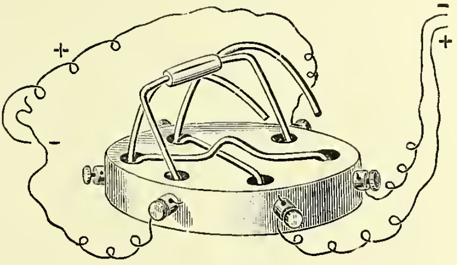
Electrodes: *A*, kaolin electrode; *z*, zinc rod; *zs*, saturated solution of $ZnSO_4$; *t*, glass tube; *K*, plug of plastic kaolin. *B*, v. Fleischl's brush electrode, in which a camel's-hair brush is substituted for the kaolin plug. *C*, Hand electrodes, made by pushing the common battery wires through rubber tubing—for insulation—and binding together with thread.

3. METHODS OF MODIFYING THE CURRENT.

It frequently becomes necessary to change either the direction, the course or the strength of the current.

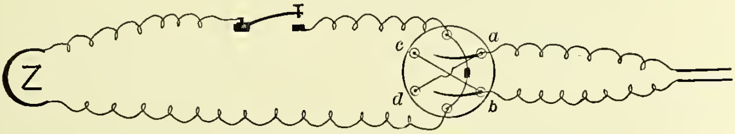
1. **To Change the Direction or the Course of the Current.**—For this a *Pohl's commutator* is generally used (see Fig. 21). The two binding posts to which the bridge is hinged may be called the "bridge-posts." The battery-wires should be joined to these posts. The cylindrical handle which is used in tipping the bridge to the right or the left is of non-conducting material. The current passes into the upright arm of the bridge, thence into the semi-circular span, whence it passes to the mercury cup into which the span dips, completing the circuit through the cross-bars when the bridge is tipped to the left (position *cd*, Fig. 22), or completing it direct when the bridge is tipped to the right (position *ab*). The change from one position to the other thus changes the direction of the current beyond the commutator.

Fig. 21.



Pohl's commutator.

Fig. 22.



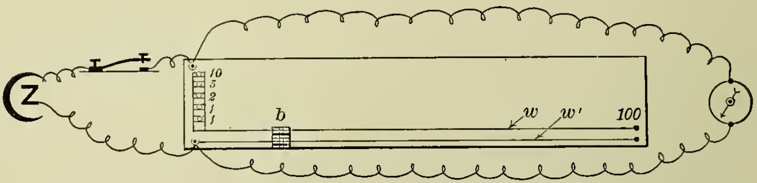
Showing use of Pohl's commutator.

If the cross-bars are removed the current may be thrown at will into a circuit joined at *ab* or one joined at *cd*, thus changing the course of the circuit.

2. **To Change the Strength of the Current.**—(*a*) The current may be increased BY THE COMBINATION OF CELLS IN A BATTERY. If the external resistance is high, which is the case in all physiological or therapeutic uses of electricity, the cells composing the battery should be joined *in series*.

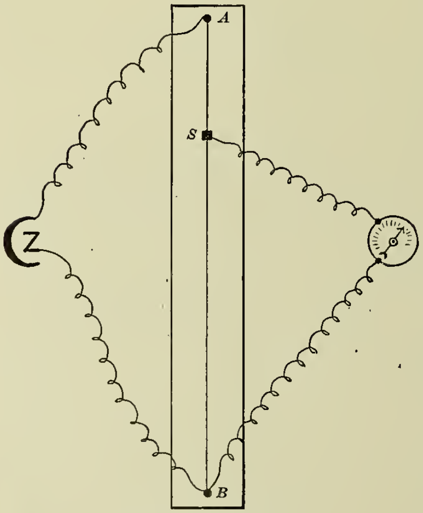
(*b*) THE CURRENT MAY BE VARIED BY VARYING THE EXTERNAL RESISTANCE $\left(C = \frac{E}{R}\right)$. This may be accomplished by joining a resistance box or rheostat in the circuit. There are two ways of doing this: (I) To join the rheostat in the long circuit, by which method a removal of the plugs will decrease the current by adding resistance to its passage; (II) to join the rheostat in short-circuit, by which method a removal of plugs will oppose an increased resistance to the short circuit, throwing more current into the long circuit. The first method causes a gradual decrease of the current from a maximum to a minimum; while the second and more generally employed method causes a gradual increase from zero to a maximum. The resistance box presents the disadvantage that the resistance is added or subtracted *step by step.* Many physiological experiments require the current to change by *infinitesimal increments.* DuBois-Reymond contrived an instument which accomplishes this result, the rheocord (Fig. 23). The DuBois-Reymond rheocord differs from the rheostat in substituting for the low resistance spools two parallel platinum wires (*ww'*) which are connected by a bridge (*b*). As the bridge is slowly moved from position 0 to position 100, the resistance of the platinum wires (1Ω) is as slowly added to the short circuit. Bringing the bridge back to the zero point and removing the plug which represents 1Ω, one may slowly slide the bridge up to 100 again adding another ohm, and so on until 15 or 20Ω have been thrown into the short circuit.

Fig. 23.



DuBois-Reymond's rheocord.

Fig. 24.



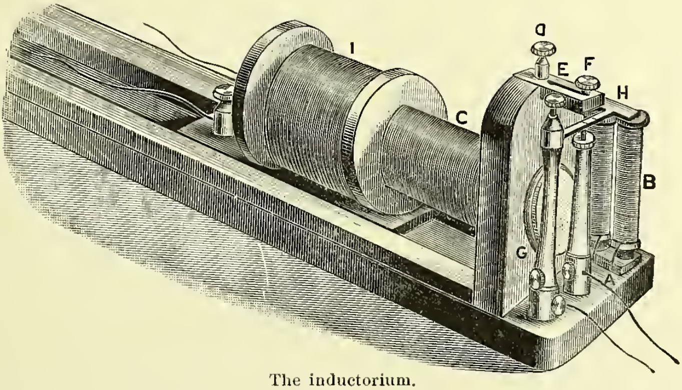
The simple rheocord.

(*c*) The Current may be varied by leading off or deriving any desired portion of the principal current. For this purpose one may use the simple rheocord. (Fig. 24.) When the principal circuit is closed the current passes from the cell to post *A* of the rheocord, along the German silver wire until it reaches the sliding contact (*s*) when two ways are open to it: (I) through the wire to *B* and back to the cell, or (II) through the galvanometer circuit. The amount of current which will pass along these two ways will be reciprocally proportional to the resistances offered by the two circuits. When the sliding contact (*s*) is in contact with *B* the derived or galvanometer current will be zero, when it is in contact with *A* the derived current will be at its maximum. The principle involved in the Ludwig compensator and in the round compensator is the same as that utilized in the simple rheocord.

4. THE INDUCTORIUM.

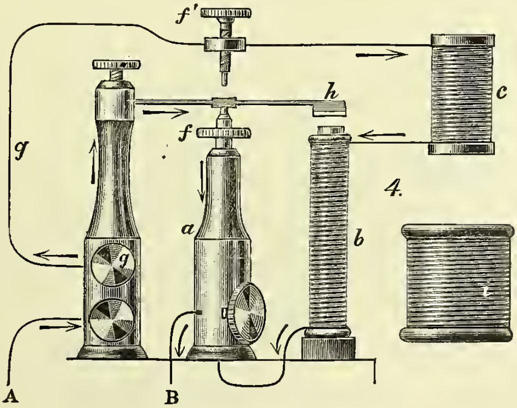
The induced current is much used in this field of experimental physiology. Several special forms of inductorium have been contrived. That of DuBois-Reymond is shown in Fig. 25. Two binding posts connect directly with the primary circuit. By connecting the battery to these an induced current is made every time the primary current is closed or opened. By connecting the

Fig. 25.



The inductorium.

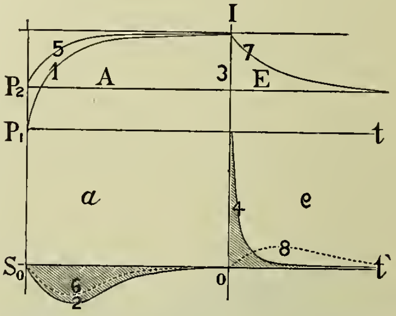
Fig. 26.



Plan of Neef's interrupter.

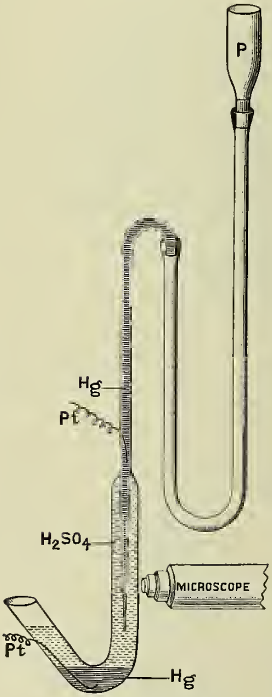
battery wires at G and A the primary current is closed and opened automatically through the reciprocal action on the electromagnet B and the elasticity of the hammer H. For a clearer plan of this mechanism see Fig. 26. But this arrangement leads to "extra currents" in the inductorium which modify the induced current as shown by the full lines of the next diagram. (Fig. 27.) Von Helmholtz contrived an arrangement by which the influence of the extra currents could be suspended and the "make" current equalize with the "break" current. The connection *g* with the screw *f* (Fig. 26) makes the primary circuit, draws the hammer down until it touches *f*, which short-circuits a portion of the primary current, weakens the magnet, releases the hammer, and again throws all of the primary current into the long circuit. Thus the primary circuit is never broken, but rapidly varies between its maximum and minimum as shown at 5 and 7. (Fig. 27.) In the meantime the induced current gives practically equal make and break shocks as shown by the dotted lines 6 and 8.

FIG. 27.



Scheme of the induced currents. P_1, abscissa of the primary, and S_0, of the secondary current; A, beginning, and E, end of the inducing current; 1, curve of the primary current weakened by an extra-current; 3, where the primary current is opened; 2 and 4, corresponding currents induced in the secondary spiral; P_2, height, *i. e.*, the strength of the constant inducing current; 5 and 7, the curve of the inducing current when it is opened and closed through Helmholtz's modification; 6 and 8, the corresponding currents induced in the secondary circuit.

FIG. 28.



Capillary electrometer.

5. MEASUREMENTS OF ELECTRICITY.

The delicate galvanometers of Wiedemann or of Thompson are familiar to the student through his work in physics. These instruments are used in physiology to measure muscle and nerve currents.

Another instrument much used in physiology is the capillary electrometer, whose construction is shown in Fig. 28. The electrometer and the microscope are so mounted that all required adjustments are made by turning fine-adjustment screws. If the two platinum wires (Pt, Pt′) are joined up with non-polarizable electrodes, and if these are touched to portions of a body which represent different electric potential, the mercury will instantly move along the capillary, the direction of its motion indicates the direction of the muscle or nerve current, and the extent of the motion indicates the strength of the tissue current.

6. METHODS OF RECORDING RESULTS.

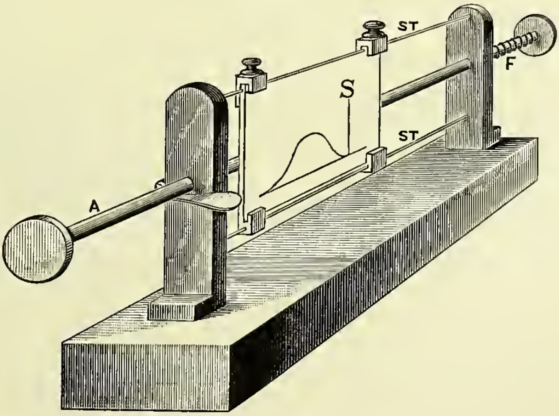
a. The Direct Method.

This method consists in the quick, inexpensive and direct observation of the results of various stimuli with tabulation of the observations.

b. The Graphic Method.

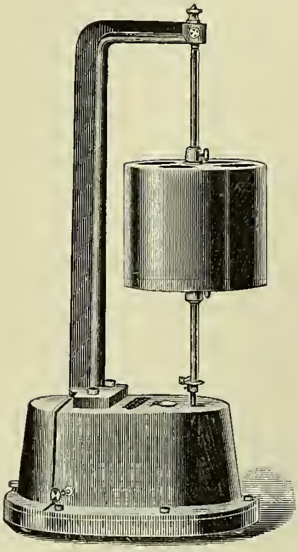
This somewhat more elaborate method is so much more satisfactory that it is now universally used in laboratory experiments. The contraction of a muscle in response to a stimulus lifts a lever whose extremity is provided with a writing point. This writing point traces the movements of the lever upon a moving surface. Various devices have been employed to furnish the moving surface; the pendulum myograph, the spring myograph (Fig. 29) and the rotating cylinder. The latter appliance has come into general use for graphically recording various movements and has

Fig. 29.



received the name *Kymograph* or *wave writer* (see Fig. 30). The instrument figured is only one of numerous forms. Some are propelled by clock-work, some by steam or electric motor, some by weight and pulley. The form of the recorded wave depends in part upon the speed of rotation of the cylinder. The height of the wave—the ordinate—depends solely on the rise of the lever; but the outline of the wave, especially its extent along the base line—its abscissa—depends upon the relative speed of two movements: (I) the rate of rotation of the drum; and (II) the rate of movement of the lever.

Fig. 30.



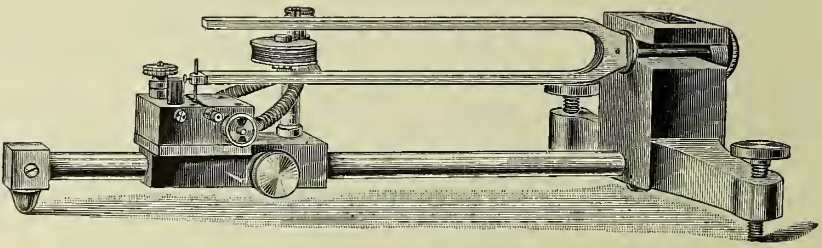
The kymograph.

c. The Time Record.

This is frequently necessary. In work upon the circulatory and respiratory systems it is sufficient to have a time record in seconds; such a record can be readily gotten from a contact clock which beats seconds, joined in circuit with a time-marker or *chronograph*. In muscular-nerve physiology it is necessary to record the time in shorter intervals.

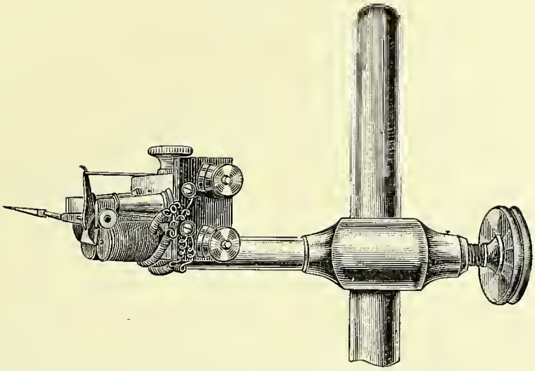
The Tuning Fork (Fig. 31), whose vibrations are maintained by an electric current, is usually used for this purpose. Vibrations numbering 50 to 200 per second may be recorded upon a moving surface by the *Deprez signal* (Fig. 32), which is joined in circuit with the tuning fork.

Fig. 31.



The tuning-fork as an interrupter.

FIG. 32.



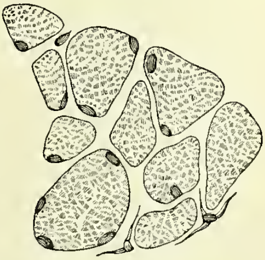
The Deprez signal.

B. ANATOMICAL INTRODUCTION.

1. THE STRUCTURE OF MUSCLE.

The unit of structure of muscular tissue is the *muscle-cell* or *muscle-fiber.* The muscle-cell is a multinuclear cell of prodigious size, some of them reaching a length of 12 cm. (Felix, quoted by Biederman in *Electro-Physiology*), while they have a diameter ranging from 0.013 to 0.019 mm., making them easily visible to the unaided eye as fine threads. If one examine a muscle he will find it to be enclosed in a sheath of glistening connective tissue—*epimysium*—and to be readily divisible into prismatic bundles or muscular *fasciculi,* each of which is in turn surrounded by a connective tissue sheath, the *perimysium.* The accompanying figure (Fig. 33) shows a cross-section of a fasciculus the perimysium not being depicted. The fasciculus is in turn composed of muscle-fibers or muscle-cells, the spaces between which are occupied by delicate connective tissue, the *endomysium.* Note the dark spots in the periphery of the fibers. These are the nuclei. Each fiber or cell is surrounded by a delicate cell-wall (Kölliker) the *sarcolemma,* shown in the figure as a thin black line surrounding each cell. As in the typical cell we have the cytoplasm divided into two fairly distinct substances—spongioplasm and cytolymph—so here we find structures which must represent their homologues, viz.: *fibrillæ* and *sarcoplasm.* In the figure the shaded areas (areas of Cohnheim) into which the cross-section of each fiber is

FIG. 33.

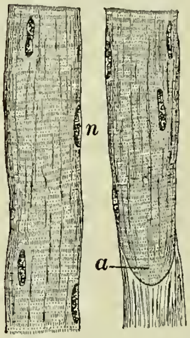


Cross-section of a fasciculus of muscle.

divided represents bundles of fibrillæ—*muscle columns*, which are separated by the sarcoplasm.

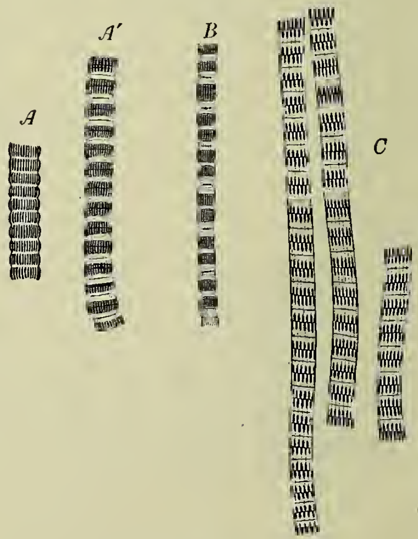
The proportion of sarcoplasm to fibrillar substance may vary enormously, alike in the muscles of different animals, and in the different muscles of the same species. * * "Those muscle fibers which serve the most persistent or most strenuous action are richest in sarcoplasm." * * "The great pectoral muscle of the best fliers (among the birds) consists exclusively, or almost exclusively, of plasmic (rich in sarcoplasm) fibers, while in the weak-winged fowls it consists predominantly of aplasmic (poor in sarcoplasm) fibers." * * * "There can be no doubt that energetic chemical changes go on in the sarcoplasm, as is proved by the frequent appearance within it of fat drops." * * * "All indications favor the proposition that *the sarcoplasm* furnishes the pabulum which nourishes the fibrillar substance during its activity." * * * "If, then, it really is the *rôle* of the interfibrillar plasma (sarcoplasm) to preside over the nutrition of the contractile substance, the greater abundance of sarcoplasm in the muscles which serves the most strenuous and persistent functions is readily intelligible.—(Quotations from Biederman's Electro-Physiology.)

FIG. 34.



Voluntary muscle, portions of two fibers showing the characteristic transverse markings; the lighter band is divided by the row of minute beads constituting the intermediate disk: *a*, termination of muscular substance and attachment of adjoining fibrous tissue; *n*, nuclei of muscle-fibers. (PIERSOL.)

FIG. 35.



Wing muscles of an insect.

The structure of the fibrilla has been a matter of investigation for many years. Many of the points at issue are still unsettled.

Fig. 34 shows a view of a human muscle-fiber under rather high magnification. Note the alternating light and dark bands;

and that the light bands are subdivided by a fine dotted line. This line is called *Krause's membrane* because it has been thought to be a membrane. The whole fiber is composed of a great number of parallel fibrillæ. Each fibrilla is segmented and presents the same alternating dark and light segments shown by the fiber as a whole. Furthermore each fibrilla possesses a portion of the "Krause membrane." It must be evident that the areas of Cohnheim represent cross-sections of the fibrillæ.

Fig. 36.

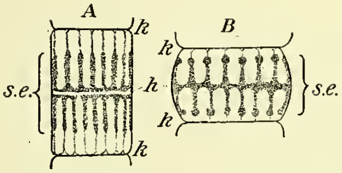
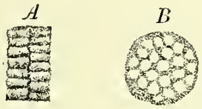


Diagram of a sarcomere. *A*, extended; *B*, contracted.

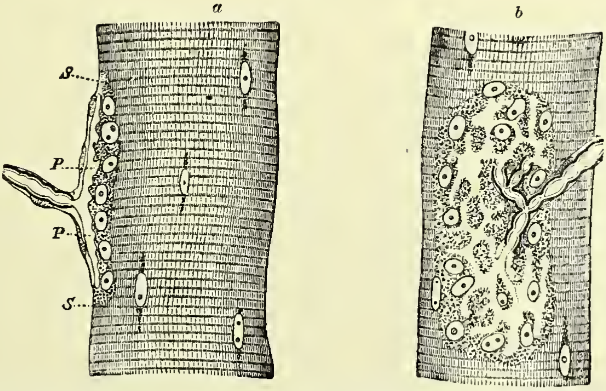
Fig. 37.



Isolated sarcous elements. *A*, side view; *B*, end view.

The most favorable material for the study of the finer structure of the fibrillæ is presented by the wing muscles of insects. Schaefer's preparations shown in Fig. 35 give a very good idea of this structure. The portion between two Krause membranes is called a sarcomere. Note that in the extended condition (*A*) the dark band has a light line dividing it transversely; this light line is called the line or plane of Hensen (see Fig. 36, *Ah*). This plane of Hensen disappears when the fibrilla is contracted (see Fig. 36, *Bh*). Each sarcomere then is occupied by dark and light matter. The dark matter seems to be more solid than the light matter. It is called a sarcous element. From the figures given

Fig. 38.

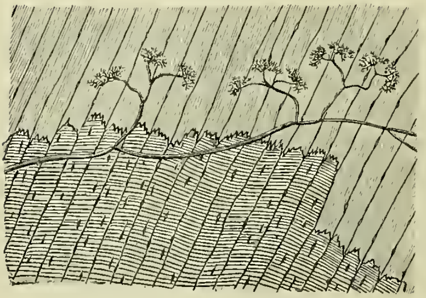


Two muscular fibers from the psoas of a guinea-pig, showing the terminations of the nerves *a*, *b*, the primitive fibers with their transition into the terminal plates, *P*, *P*. Note neurilemma with nuclei, continuous with the sarcolemma. Note nuclei in muscle. (After McKendrick.)

one cannot see just how the matter of the sarcous element is disposed but an end view (Fig. 37, *B*) shows it to be porous and that the white matter takes the form of cylindrical extensions which fill the pores. Halliburton looks upon the sarcous element as representing spongioplasm and the clear substance as representing the hyaloplasm (cytolymph).

The blood supply of the muscle is distributed as fine capillaries which occupy spaces between the fibers but never pierce the sarcolemma. The nerves, however, terminate in end-plates which lie within the sarcolemma (see Fig. 38). There are nerve-endings in the tendons also. These nerves are sensory nerves and are stimulated by sudden change of tension upon the tendon. Fig. 39 shows this as well as the way in which the muscle fibers pass into tendon fibers.

Fig. 39.

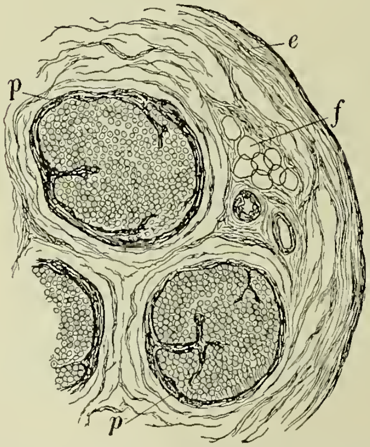


Nerve endings in tendon.

2. THE STRUCTURE OF NERVES.

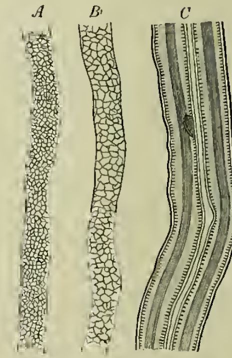
A *nerve-trunk*, such as one finds in his dissections is constructed as shown in Fig. 40, with a loose connective tissue sheath

Fig. 40.



Section of portion of a nerve-trunk including three bundles, or funiculi, surrounded by the perineurium (*p*); the funiculi, together with the blood vessels and adipose tissue, are united by the more general epineurium (*e*); the sections of the individual nerve-fibers are held in place by the endoneurium; *f*, fat-cells, near which are the sections of blood vessels. (After PIERSOL.)

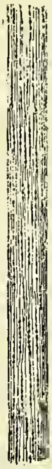
Fig. 41.



Medullated nerve fibers. *A* and *B* surface views of sheath and white substance of Schwann, *C* optical section showing fibrillated structure of the axis-cylinder.

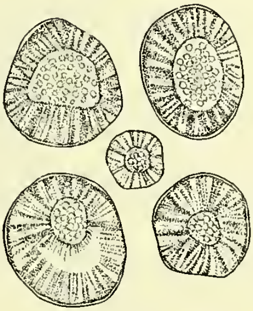
(epineurium) surrounding and separating the *nerve-bundles*. Each bundle is ensheathed in *perineurium* which sends extensions of *endoneurium* into each bundle. The bundles consist essentially of a great number of nerve fibers. A medullated nerve fiber (see Fig. 41) is composed essentially of an axis-cylinder surrounded by the medullary sheath or white substance of Schwann, which is in turn enclosed in the primitive sheath. The axis-cylinder is composed in turn of fibrillæ (see Fig. 42). The fibrils seem to be separated by a ground substance as shown by Schaefer (Fig. 43).

FIG. 42.



Axis-cylinder, highly magnified. showing the fibrils composing it, (SCHAEFER, after M. SCHULTZE.)

FIG. 43.



Section across five nerve-fibers. (Magnified 1000 diameters.)

The nerve was hardened in picric acid and stained with picro-carmine. The radial striation of the medullary sheath is very apparent. In one fiber the rays are broken by shrinkage of the axis-cylinder. The fibrils of the axis-cylinder appear tubular. (SCHAEFER.)

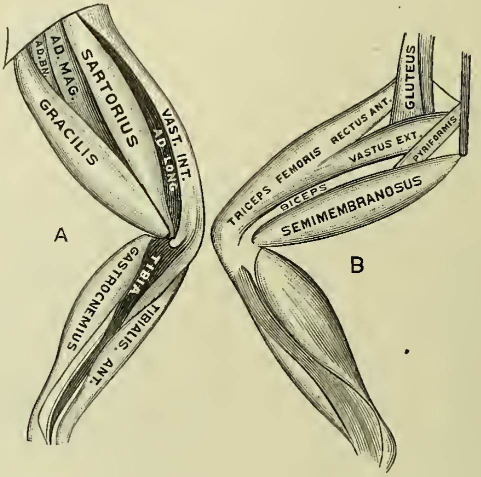
3. THE MUSCLE-NERVE PREPARATION.

The general principles of the physiology of contractile and irritable tissues are universally demonstrated with the tissues of a frog. Various muscles and nerves are used for these experiments but the one most used is the gastrocnemius muscle with the sciatic nerve which supplies it.

The accompanying figure shows sufficiently the anatomy of the frog's leg.

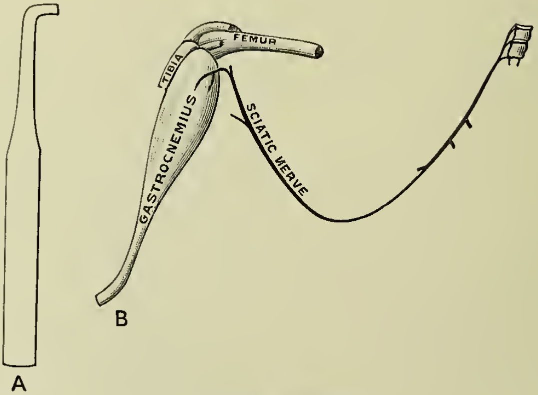
To make a muscle-nerve preparation one destroys the brain of the frog (piths it) pins it dorsum upwards upon a cork board and removes the skin from the leg, thigh and pelvic region. If the small, glistening tendon of the biceps be severed, where it is inserted upon the tibia, and the muscle dissected out and removed one will find below where it lay the large trunk of the sciatic nerve with the accompanying blood vessels—sciatic artery and sciatic and femoral veins. If the urostyle be removed the sciatic plexus will be revealed so that by gently lifting the nerve with a fine glass rod it may be easily dissected out from its spinal origin to the gastrocnemius. The rest of the dissection required to produce the preparation as shown in Fig. 45 is readily made, the femur may be clamped to a support and the tendon attached to the

Fig. 44.



Showing anatomy of the frog's leg. *A*, ventral; *B*, dorsal view.

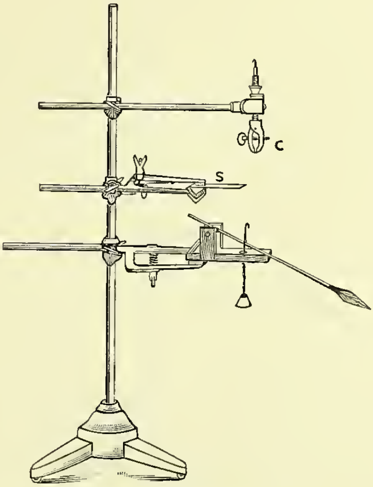
Fig. 45.



A, glass nerve-hook for lifting a nerve while dissecting it out; *B*, muscle-nerve preparation as it appears when completed.

lever of a myograph through a hook or thread. (See Fig. 46.) Contraction of the muscle will raise the lever, and the latter may be made to trace its movements graphically upon a rotating cylinder or kymograph.

FIG. 46.



The simple myograph.

THE PHYSIOLOGY OF CONTRACTILE AND IRRITABLE TISSUES.

A. THE PHYSIOLOGY OF MUSCLE AND NERVE.

In the following brief summary of electro-physiology facts and principles of fundamental importance only will be presented—facts which may be utilized in subsequent work in physiology, pharmacology, electro-diagnosis, and electro-therapeutics.

1. STIMULI.

While one is dissecting out a muscle-nerve preparation he is certain to notice several muscular contractions, caused usually by the severing of the nerve or of some of its branches, or by various conditions present during the preparation. If one mount the preparation in the myograph, letting the nerve rest upon the glass-slide, he may further test the effect of mechanical stimuli. The muscle responds when the nerve is severed with knife or scissors; it responds if it is pinched with forceps or pricked with a needle. If the muscle is exposed to the atmosphere it will begin after a time to contract rather spasmodically when there is no apparent stimulus; the contractions increase in extent and frequency until the muscle is practically tetanized. What has been taking place? The dry atmosphere has taken up the water from the tissue plasma, leaving the salts in concentrated solution; these salts may have caused the contractions of the muscles. Apply a strong solution of common salt to the nerve of a fresh preparation, and it will begin, almost at once, a series of contractions quite like those described above, producing a "salt-tetanus." By applying glycerine to a fresh nerve a similar result is obtained. Such stimuli are called chemical stimuli.

If a fresh nerve be touched with a hot wire a response is elicited from the muscle. Temperatures between 0° C. and 100° C. do not produce contractions of the muscle unless there is a sudden change from one of the extremes to the other. Extreme temperatures only are efficient stimuli.

If while dissecting out a muscle-nerve preparation with a silver probe and steel scissors, one touch the two instruments together when both are in contact with the tissues of the frog, a vigorous contraction will be observed. The conditions were such as to cause the passage of an electric current from one metal to the other through the tissues of the frog. The tissues responded to the stimulus with a contraction. Mount the preparation and lay the nerve across the electrodes of a Daniell cell. Every time the circuit is "made" with the contact key the muscle contracts; every time the circuit is "broken" the muscle contracts, but it does not usually contract during the passage of a current. These stimuli have all been applied to the nerve (indirect stimulation); one may apply the same stimuli to the muscle itself[1] (direct stimulation), and will elicit a response in most cases, though it soon becomes evident that the muscle is not as sensitive to the various stimuli as the nerve is. In the case of the glycerine the muscle does not respond at all. An important law of electro-physiology may be readily demonstrated at this point. If a curarized sartorius muscle be ligatured in the middle tightly enough to sever the muscle substance but leave the connective tissue intact; and if this muscle be fixed in the middle, leaving the two ends free to fasten to levers, one can stimulate the two segments of the muscle and note the effect of the two poles, *anode* and *kathode.* Nonpolarizable electrodes should be used for this purpose, and one should touch each segment of the muscle. If one segment contracts on make it is the kathode segment; if only one segment contracts on break it is the anode segment. Reverse the current with a Pohl's commutator and the same is true—the make contraction is kathodic and the break contraction anodic. If both contract on making the current, the kathode segment begins first; if both contract on break the anodic segment begins first. The following laws of electrical response may be formulated: *Law I. The make stimulus is kathodic; the break stimulus is anodic. Law II. The "make" or kathodic stimulus of a current is more irritating to nerve or muscle than the "break" or anodic stimulus.*

A question which naturally arises very early in the study of various stimuli is: Does the way in which a given stimulus is applied to a nerve affect the response which the muscle gives? If one gently tap a nerve which is lying upon a glass plate a slight contraction of the muscle will follow. A somewhat harder tap will cause a somewhat more vigorous response, but the maximum response is soon elicited. After that any increase in the strength of the stimulus will not cause an increase in the response. In a similar way a very weak electrical stimulus will cause a weak response, a stronger stimulus, a stronger response, etc.; but the maximum response is elicited with what is really a very mild stimulus, beyond this maximum response any increase of stimulus will not elicit a greater response.

Another way of varying the stimuli is to vary the time of application or the rate of change of conditions. One may sever or crush a nerve so slowly that the muscle will not respond. One may raise the temperature so slowly that the nerve may be cooked without having called forth a response, one may, through the

---

[1] First paralyze the nerve-endings of the muscle by curarizing the frog.

Fleischl rheonom, send an electric current into a nerve so slowly that the muscle will not respond. The general principles here illustrated may be thus summarized:

(*α*) There are four kinds of stimuli: (I) Mechanical; (II) Chemical; (III) Thermal; (IV) Electrical.

(*β*) Whatever stimulus be applied to a specialized sensitive tissue the response is the same in general character, *i. e.*, muscle always responds by contraction.

(*γ*) The strength of the response may vary with the strength of the stimulus, but it is not at all proportional to the strength of the stimulus.

(*δ*) A stimulus may be applied to a nerve so slowly that there is no response on the part of the muscle.

2. CHANGES WHICH TAKE PLACE IN A MUSCLE IN RESPONSE TO STIMULI.

After having watched the response of muscle tissue to the stimuli discussed in the preceding section the following facts must have become evident: (I) Muscle-tissue is irritable; (II) Nerve-tissue is irritable; (III) Muscle-tissue transmits a stimulus from one part of a muscle to another; it, therefore, possesses the power of conductivity; (IV) Nerve-tissue possesses the power of conductivity; (V) In response to stimulus a muscle changes its form.

In the light of the experiments and discussions which have preceded, one may form a general conception of what takes place in contractile and irritable tissues in response to a stimulus. (I) Some internal change (chemical) occurs in the nerve at the point where the stimulus is applied; this internal change is the invisible manifestation of the irritability of the nervous tissue. (II) The internal change begun at the point of stimulation is propagated along the nerve trunk; indeed, along the axis-cylinders, because the nerve loses its insulating sheath before it reaches its final distribution. (III) It is transmitted to the individual muscle-fibers through the end-plates of the nerves which lie just within the sarcolemma of each fiber. (IV) It is propagated through the contractile substance of the fiber, so that all the fibers of the muscle contract at practically the same time. (V) There are internal changes in the muscle and nerve, which accompany the more evident change of form which takes place in the muscle.

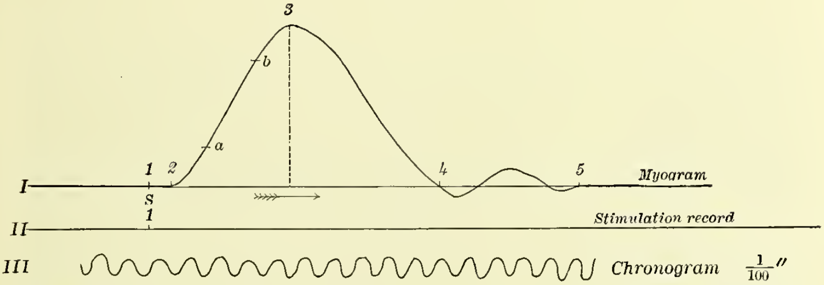
These internal changes are: Chemical, thermal and electrical, as subsequent observation will demonstrate.

a. Change in Form.

1. **Change in Length.**—In studying the change in form which a muscle undergoes incident to its response to a stimulus it

is customary to mount a muscle-nerve preparation in a myograph whose lever may trace upon a kymograph any changes in length which the muscle may undergo. Almost any efficient stimulus may be used; the only requirement being that in its application to the nerve it must be sudden in its beginning, instantaneous in its duration, and sudden in its cessation. It is impossible to fill these requirements with chemical or thermal stimuli; but possible to do so with various mechanical and electrical stimuli. It is customary to use electrical stimuli. The "break" induction shock is especially adapted to this purpose.

Fig. 47.

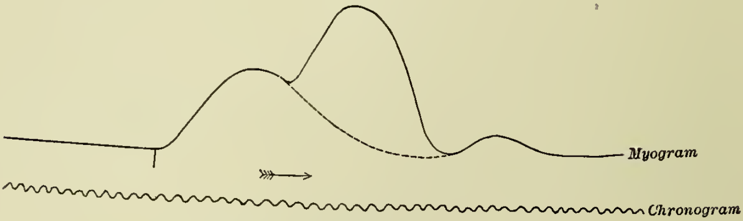


Tracing of single muscular contraction. 1–2, latent period; 2–3, period of contraction; 3–4, period of relaxation; 4–5, period of elastic after-effect.

(*a*) As the Result of One Shock the muscle in contraction will trace upon a rapidly moving surface such a curve as is shown in Fig. 47. Such a tracing of a single muscular contraction reveals certain important facts regarding the response of a muscle to a stimulus. (I) On abscissa *II* (*s*) indicates the time of stimulation. Note that muscle, whose lever was tracing abscissa *I*, did not begin to shorten until about $\frac{1}{100}$ of a second had elapsed. This is called the *latent period*. (II) The period of contraction shows a slight acceleration at first, followed by a period of maximum rate of shortening (between *a* and *b*) after which there is a retardation of the rate of shortening until at 3 the apex of the curve is reached and for an instant retains this position of maximum contraction. (III) The period of relaxation follows immediately, but the rate of relaxation is less rapid at the beginning of this period than toward the end. Note that the period of relaxation (3–4) is longer than the period of contraction. (IV) If the muscle is moderately loaded and the lever without a rest or stop the muscle will relax beyond its original position of rest; that is, the curve will pass below the abscissa, but will instantly recover itself coming above the abscissa. This is simply an after-effect due to the elasticity of the muscle and to the general conditions to which it is subjected.

(*b*) Suppose a muscle be given *a second stimulus* before it has had time to complete its response to the first, what will the result be? Fig. 48 shows the typical result as traced by Foster. (I) Note that the crest of the second wave is higher than that of the first. (II) The contraction of the second is more rapid and its relaxation more rapid than observed in the first contraction.

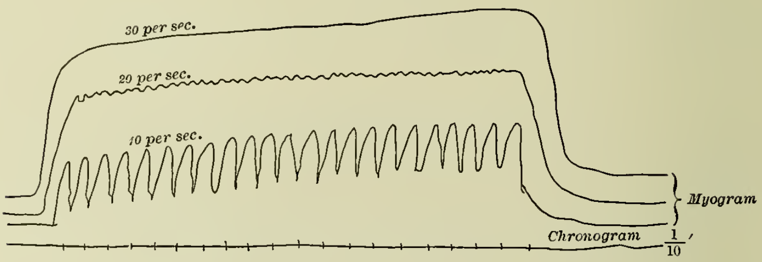
FIG. 48.



Tracing of a double muscle curve. (FOSTER.)

(*c*) THE SUMMATION OF THE EFFECTS OF STIMULI is well illustrated in Waller's figure (Fig. 49). With a comparatively slow moving cylinder and stimuli given at the rate of ten per second the lever will drop back nearly to the abscissa, to rise again with another stimulus. With twenty shocks per second the lever remains nearly stationary. With thirty shocks per minute the lever traces a perfectly straight line. This is a tetanus of the muscle. Tetanus is a sustained contraction of a muscle caused by a series of rapidly repeated stimuli. One may voluntarily bring a muscle into a state of sustained contraction. Though one is not conscious of the process which is going on in the nerve and muscle he may infer from the foregoing that during sustained contraction there is a series of rapidly repeated stimuli passing from the central nervous system to the muscle. The greatest number of voluntary movements which one can make in a second is limited to eight or ten. The observations of Schaefer and of von Kries show "that the graphic record of even the steadiest voluntary

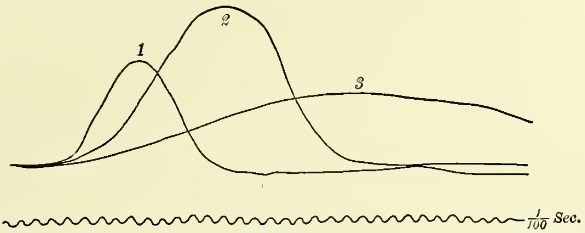
FIG. 49.



Summation of contractions: composition of tetanus. (After WALLER.)

movement exhibits a tremor" of 8 to 12 vibrations per second (Waller).

FIG. 50.



The effect of temperature upon muscular contraction. 1, normal; 2, cooling; 3, very cold. (WALLER.)

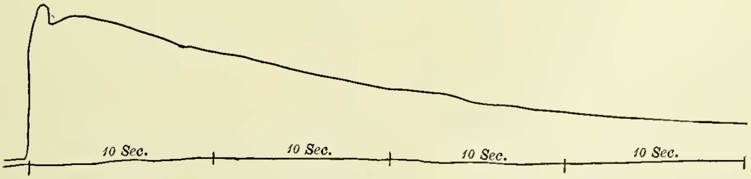
It is generally accepted that in a sustained voluntary contraction the impulse-frequency is about 10 per second. Involuntary contractions are slower in rhythm; the heart-beat represents not a tetanic condition of the ventricles but a "long twitch." Conclusive evidence of this is shown in the fact that only one change of electric condition occurs in the heart muscle at each contraction.

(*d*) THE FORM OF THE MUSCLE CURVE IS MODIFIED BY THE TEMPERATURE OF THE MUSCLE. When the temperature is only a little below normal the latent period is longer, the rise less sudden. When the temperature is very low the contraction and relaxation are both much prolonged and the shortening much less than normal. (See Fig. 50.)

(*e*) If a muscle be subjected to *a series of equal stimuli at short intervals* (6 to 10 per sec.) each one of the first 10 or 12 contractions will be higher than the previous one, giving rise to the so-called "*staircase*" myogram. This seems to indicate that one response better fits the muscle for successive ones.

(*f*) THE MUSCLE-CURVE IS MODIFIED BY DRUGS. Fig. 51 shows the effect of veratrin. Notice that though the contraction is about as sudden as usual the relaxation is much retarded—forty seconds not sufficing to bring the lever back to the abscissa.

FIG. 51.



Effect of veratrin upon the myogram. (WALLER.)

(*g*) THE MUSCLE-CURVE IS MODIFIED BY THE LOAD which the muscle must lift. A moderate load is likely to act as a supplementary stimulus to a muscle causing it to contract more with the load than without it, as the load is increased, however, two modifications may be noted in the myogram; (I) The latent period is longer because more time is required to generate sufficient energy to overcome the inertia of the load. (II) As the load increases the curve becomes progressively lower though the actual work done may be greater.

2. **Change in the Transverse Dimensions of the Muscle.**—The volume of the muscle remaining practically the same there must be an increase in the transverse dimensions sufficient to compensate for the decrease in the length of the muscle. This thickening of the muscle may be recorded in two ways: (I) by resting the muscle on a horizontal plate or within a shallow horizontal trough and resting a tracing lever upon its upper surface; (II) by clasping the muscle gently in a forceps-lever and transmitting the movement through a pair of Marey tambours.

If one places a lever at each end of a long muscle like the sartorius it becomes at once evident not only that there is a thickening of the muscle during contraction, but that the thickening progresses as an undulation from one end of the muscle to the other when the muscle is stimulated at one end. The rate of propagation of this wave has been measured and is equal to from 1 to 3 meters per second according to the various conditions of the experiment.

3. **The Work Done by a Contracting Muscle.**—The conditions under which most muscular contractions are studied as outlined in the foregoing paragraphs make it easy to estimate the work which the contracting muscle actually performs. Work done equals the product of the weight raised and the height through which it is raised. ($W = g \times h$.) If a muscle lift 100 gms., 5 mm. the work equals 50 gm.-cm. If a strong muscular contraction fail to lift a weight no work is done though energy has been liberated in the muscle. If a loaded muscle be thrown into tetanus work is done only when the lever is raised, and not during the time when the weight is sustained. Energy is liberated, however, and the muscle is fatigued, but the energy does not take the form of mechanical work in the technical sense of that term.

The amount of work which a muscle can perform varies according to several factors.

(*a*) WORK IS MODIFIED BY THE STRENGTH OF THE STIMULUS. The weakest efficient stimulus will cause a series of contractions lifting a given weight through a very short distance. This minimum efficient stimulus is also termed the "stimulus of *liminal intensity.*" Let the stimulus be gradually increased, the height of contraction will be rapidly increased to a maximum. The stimulus whose intensity is just great enough to cause the maximum contraction is called the "stimulus of *optimum intensity.*" Let the stimulus be increased; the contraction will not be greater, on the other hand it is likely to be less because of fatigue from over-stimulation.

(*b*) WORK IS MODIFIED BY THE INTERVAL OF TIME which elapses between the stimuli. The minimum interval, just short of a tetanic contraction, is unfavorable to the muscle because there is a rapid accumulation within the muscle, of carbon dioxide, sarcolactic acid, etc., which cause the rapid fatigue of the muscle. The optimum interval is such that the products of katabolism incident to the liberation of energy may be carried away from the muscle by the circulation. There can hardly be an optimum interval, then, for a muscle which has been removed from the organism. There is, however, an interval most favorable under the conditions, and that interval is from 1 to 3 or 4 seconds.

(*b*) WORK IS MODIFIED BY THE LOAD. (*α*) The disposition of the load: (I) If a weight is simply hung upon the lever it stretches the muscle even when the latter is at rest; this tends to exhaust the muscle somewhat and it cannot accomplish so much as if "after-loaded." (II) If the lever comes to a rest at the end of the relaxation of the muscle there is no stretching of the muscle between contractions. This is called "after-loading" a muscle. The short period of absolute repose between contractions is advantageous to the muscle.

(*β*) The amount of the load also modifies the amount of the work which a muscle is able to accomplish. A muscle will lift a hundred grammes as high as it will lift one gramme, thus doing one hundred times as much work in one contraction. The total work done in a series of contractions leading to fatigue will be greater for medium (50 gms. to 100 gms.) weights than for heavy weights (200 gms. to 250 gms.) though the work of one contraction may be two or three times as great in the case of the heavier load.

(*c*) WORK IS MODIFIED ALSO BY THE DIMENSIONS OF THE RESTING MUSCLE. The extent of a contraction varies with the length of the contracting fibers; while the strength of the contraction varies with the number of the contracting fibers, *i. e.*, with the sectional area of the muscle. Both of the work factors ($g \times h$) are modified by the two factors of the muscle volume: sectional area (a) and length (l); that is, g varies as a, and h varies as l, therefore, $g \times h$ varies as $a \times l$ or W varies as $a \times l$.

b. Chemical Changes which take place in a Contracting Muscle.

The chemical composition of dead mammalian muscle tissue is approximately as given in the following table:

Water	75%—77.5%
Solids	25 —22.5
Nitrogenous	21 —22
Proteid	18 —20
Nitrogenous metabolites	about 1
Kreatin, Xanthin, etc.	
Non-nitrogenous	about 0.5— 1
Carbohydrates	0.5— 1
Inosit	trace
Inorganic (carbonate and phosphate of K and Na)	about 1

The difficulty of determining just what chemical changes take place in a living muscle incident to its activity must be evident. The only index of these changes which present methods make possible is analysis of dead muscle that has been at rest and of dead muscle that has been fatigued just before being killed. Analysis of the gas consumed and given off by a resting or contracting muscle also affords data. From these various methods it has been conclusively determined that contracting muscle produces: (I) more carbon dioxide, and (II) more sarcolactic acid; and that it consumes: (I) more oxygen, and (II) more glycogen.

In this connection it is important to note that the muscle is chemically active when it is apparently at rest. Muscular tissue is the most important heat producing tissue of the body. Heat production continues while the muscle is quiescent. This constant heat production is in part at the expense of the proteids of the muscle plasma (sarcoplasm) as well as of the proteids of the sarcous elements. The katabolism of these nitrogenous substances yields a series of nitrogenous katabolites, among which may be enumerated: Kreatin, xanthin, glycocoll, ammonium lactate.

The reaction of muscle changes with vigorous activity. Resting muscle is faintly alkaline or amphicroic because of the potassium and sodium carbonates and phosphates present. Accumulation of carbonic and sarcolactic acid in the muscle soon changes the reaction to a distinctly acid one.

The chemical changes which take place in muscle will be further discussed under Physiology of the Muscular System.

c. Thermal Changes Which Take Place in Contracting Muscle.

The chemical changes above enumerated are, in largest part, oxidations, leading to the production of considerable quantities of CO_2. But such changes are always accompanied by the evolution of heat not less surely in muscle than in a furnace. Vigorous and continued contractions produce considerable heat. One's impulse to be more active in cold than in warm weather is in response to the need of the organism for more heat. Heat is constantly liberated in muscle tissue, but more is liberated when the muscle is actively contracting than when at rest. This may be demonstrated by the use of thermo-electric couples, one set of which may be introduced into the gastrocnemius of one side, the other set into the other gastrocnemius, while the long connecting circuit passes to a galvanometer. (See Fig. 52.) Any increase in the temperature of the contracting muscle is indicated by a deflection of the galvanometer needle. This arrangement enables one to demonstrate the liberation of heat in contracting muscle. The second needle may be placed in a liquid whose temperature may be raised or lowered to bring the galvanometer needle to rest at the zero position; the temperature of the liquid may be determined by a delicate thermometer. Multiplication of the number of couples of needles makes the apparatus more delicate. Heidenhain gives the rise of temperature for one contraction of a frog's gastrocnemius as 0.001 to 0.005 of a degree Centigrade; and Helmholtz found a rise of temperature amounting to 0.14°–0.18° C. after two or three minutes of tetanization.

Fig. 52.

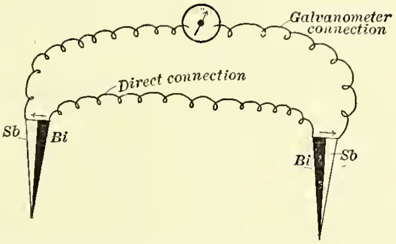


Diagram of thermo-electric couples. When both couples have the same temperature the galvanometer needle remains at rest.

d. Electrical Changes which Take Place in Muscle.

In the process of dissecting out a muscle-nerve preparation one is likely to drop the cut-off central end of the sciatic nerve upon the gastrocnemius muscle. Should this occur a contraction of the muscle is almost sure to take place. Galvani performed this experiment and cited it as a proof that electricity exists in animal tissues. Follow the line of experimentation. Make two preparations, lay them upon a glass plate, place the nerve of preparation *a* upon the muscle of preparation *b*, so that it shall touch two well separated regions, but not the intermediate portion of the muscle. The muscle of preparation *a* will contract when the contact is made, and it will probably repeat the contraction several times on subsequent contacts. Stimulate preparation *b* while the nerve of *a* lies upon it in contact at two points; the muscle of *a* contracts with every contraction of *b*. This is called a secondary contraction, and preparation *a* which contracts secondarily is called a *rheoscopic preparation* or a "*physiological rheoscope.*" What is it in the cut-off nerve that causes a contraction of its muscle; What is it in a dissected-out muscle (*b*) that causes a contraction of a second preparation (*a*); or in the contracting muscle (*b*) that causes a contraction of the muscle whose nerve lies upon it? The stimulus which elicits a response from the rheoscopic preparation (*a*) can not be mechanical. It must be chemical, or thermal, or electrical. If electrical, it should be detected through the use of the galvanometer or electrometer. Place upon the center and end of a muscle contracting from mechanical stimulus, non-polarizable electrodes which are connected with a galvanometer or electrometer and a deflection of the galvanometer needle or a change in position of the mercury maniscus of the electrometer demonstrates the presence of an electrical current or better a difference of electrical potential of the two regions of the muscle. This difference of electrical potential was the stimulus which caused the secondary contraction of the rheoscopic preparation. But the latter contracted also when touched to the resting muscle. It was once supposed (DuBois-Reymond) that the difference of electrical potential exists in all muscles at rest, and the terms, "current of rest," and "current of action," were used, Hermann demonstrated, however, that a resting muscle when uninjured has no current and that injury induces a current in a general way proportional to the extent of the injury. The term "current of rest," then became misleading and was displaced by the term, "*demarcation current*" or "*current of injury.*"

It has been found that: (I) *Normal Muscle at rest is iso-electric, i. e.,* gives no evidence of a difference of electric potential in different regions. (II) *Local injury induces a difference of potential,* instantly indicated by the galvanometer or electrometer. (III) *Local action induces a difference of potential,* indicated by the galvanometer or electrometer. The current of a galvanic cell passes from the zinc plate to the copper plate,—from the plate where there is chemical action to the plate where there is no chemical action. The current of an injured muscle passes from the injured portion to the normal portion, *i. e.,* from the portion where there is much chemical action toward the portion where there is little chemical action.

The current of action is, in the same way, from the portion most active to that least active.

Both of these factors may be at work at the same time; *i. e.,* an injured muscle may be made to contract. The current of injury passes through the galvanometer from the normal to the injured portion. The point of injury is the point of least activity, that is, the change from rest to action will be greater at the normal part. Therefore the current of action will pass through the galvanometer from the injured to the normal. Thus stimulation of an injured muscle will cause the needle to swing back toward the opposite direction. This phenomenon is called the *negative variation.*

These relations are represented diagrammatically in the accompanying figure. (Fig. 53.)

If the electrodes be placed one upon the base of the ventricle and one upon the apex of the ventricle of the heart there will follow a double variation with each heart cycle. In the first phase of the cycle the base is negative to the apex, in the second phase of the cycle the apex is negative to the base, thus leading to the term, "diphasic variation" of the heart.

In this connection it may be stated that all active tissues manifest the presence of difference of potential in different regions. For example, the outer surface of the hand is negative to the inner surface; the fundus of a gland is negative to the hilus; the optic nerve is negative to the cornea, etc.

FIG. 53.

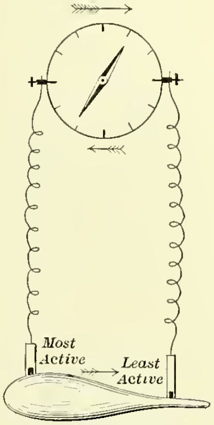


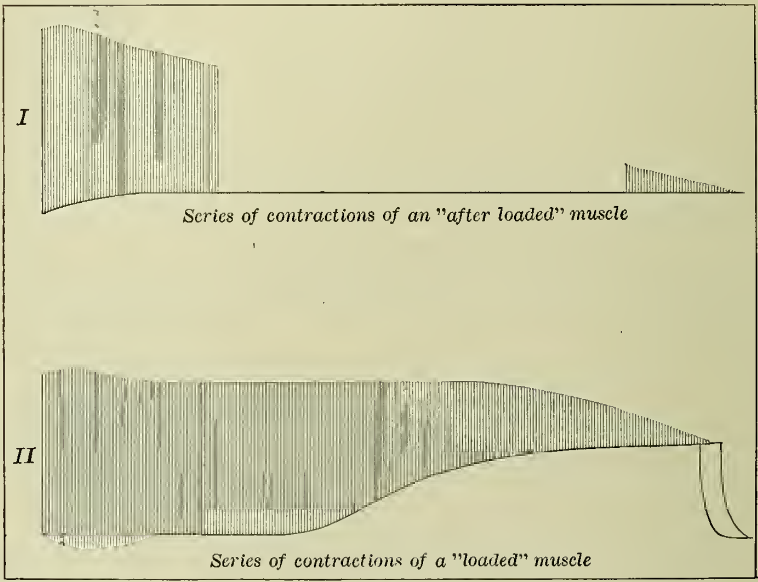
Diagram showing direction of the "current of injury" (⟶) and of the "current of action" (⟶). Also the "negative variation" of needle during action of injured muscle.

e. Fatigue.

In response to various stimuli muscle tissue undergoes changes in *form*, in *temperature*, in *electrical* condition, all of these forms of energy being liberated through the *chemical* changes which accompany them. Mention has been made above of the accumulation in the muscle of the products of the chemical changes; also of the gradual decrease in the height of successive contractions after the muscle has been contracting many times. These two phenomena are the distinctive phenomena of fatigue and the first is the cause of the second. The accumulation of the products of chemical action is the cause of the progressively decreasing power of the muscle.

The decreasing power of the muscle manifests itself by a decreasing height of the contraction waves. Just at first the waves may increase in height, the *stair-case contractions*, then there will be a greater or smaller number of waves of nearly the same length; finally, after a variable time, the waves begin to shorten up until there is no response to the recurring stimuli. Then the muscle is said to be fatigued. The conformation of the series of fatigue waves will vary considerably with the way in which the load is disposed. Fig. 54, *I*, shows a typical fatigue tracing from an "after-loaded" muscle, while *II* shows that from a "loaded" muscle. In the latter the stretching during the period of rest irritates the muscle and brings it finally into a state of typical tetanus. The fatigue is postponed by taking an optimum or at least advantageous rate of stimulation. If the stimuli come in too rapid succession fatigue is hastened. If a fatigued muscle is given a few moments respite or rest, it recovers in part and will respond vigorously to subsequent stimulation, but tires very quickly again. A muscle which is in its normal situation, receiving the benefit of exchange of material through the circulation, will accomplish much more work before fatiguing than will be the case with an excised muscle. Furthermore, the intact muscle will recover in a short time, while the excised muscle makes only a moderate recovery through the removal of CO_2 by diffusion. Fatigue is accompanied by a decrease of extensibility and elasticity, in common words a stiffness.

Fig. 54.



Showing the effect of disposition of load on the contraction of muscle modifying the amoun. of work done.

f. Rigor.

After the death of a muscle it undergoes certain changes which are similar to those which take place during fatigue; namely, the accumulation of CO_2 and of sarcolactic acid. Accompanying these chemical changes there is the "stiffness of death,"—*rigor mortis*,—due to the coagulation of the myosin. If fresh muscle substance be coagulated by heat,—50° C. to 60° C.,—there will also be a formation of CO_2 and sarcolactic acid, accompanied by the "stiffening of heat" or *rigor caloris*. The three processes; viz., fatigue with the decrease of elasticity, rigor mortis and rigor caloris, are closely related both physically and chemically.

3. THE RELATION OF THE NERVE TO VARIOUS STIMULI.

The living nerve in its normal position in the animal body functions as a conductor of impulses. These impulses may arise in the central nervous system and be conducted to various peripheral organs; or they may arise in various peripheral (sense) organs and be conducted to the central nervous system. In either case the nerve neither adds to nor subtracts from the original impulse which it receives but transmits it along the course of the nerve from one end to the other. Just how these impulses are transmitted is unknown. One can follow the steps of the chemical changes that are propagated along a fuse or of the physical changes that are propagated along a wire conductor of electricity, but the physical and chemical changes which are propagated along the axis-cylinder of a nerve are still unknown quantities as to their exact nature. It is generally accepted that they are ultimately chemical and that the initiatory chemical (metabolic) changes are accompanied by electrical changes, probably also by thermal changes.

a. The Properties of Nerve Trunks.

The fundamental and essential property of a nerve trunk is conductivity. The experiments which are described above make it evident that a nerve trunk is not only a conductor of an impulse, but that a stimulus in any part of its course may start from that point a change which will be propagated apparently in a perfectly normal way, to the normal terminus of the nerve and there transmitted to the structures normally receiving impulses from the nerve. For example, an injury or an electric shock to the sciatic nerve sets into operation at the point of the stimulus a change which is propagated to the muscles supplied by the nerve, and these structures give the normal response to the impulse. The second property of a nerve is irritability or excitability.

b. Conductivity.

The rate of propagation of an impulse along a nerve may be determined by stimulating a nerve near to its muscle, or five or six centimeters farther away from the muscle. The response to the stimulus must be recorded upon a rapidly moving surface, such as the spring myograph (Fig. 29), and the time in hundredths of a second must be recorded upon the same surface by a tuning fork (Fig. 31), the difference in time elapsing between stimulus and response in the two cases is the time required to traverse the five or six centimeters of extra nerve. In this way the rate of propagation or conduction may be determined. This method of experimentation has given the following results: Helmholtz found the rate of transmission in the motor nerves of a frog to be 27 m. per second. The rate of conduction in sensory nerves is about 35 m. per second.

The conductivity of a nerve is decreased by low temperature and increased by high temperature.

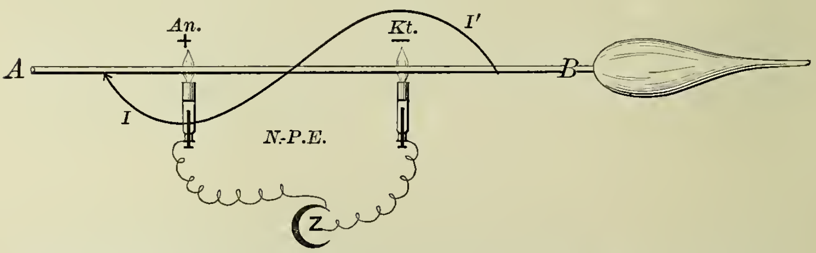
The conductivity may be destroyed by the direct application of alcohol or ether to the nerve trunk while its irritability will not be much affected. "Carbon dioxide may destroy the irritability, though leaving the conductivity unimpaired." (Lombard.)

A strong constant current decreases the conductivity of a nerve in the region of the anode during the passage of the current and in the region of the kathode after removal of the current. This modification of conductivity may be called *Law III.* of electrotonus; *Laws I.* and *II.* were given above.

c. **Irritability.**

If a constant current traverse a nerve entering and leaving by non-polarizable electrodes the nerve will be thrown into a state called *electrotonus.* The condition of electrotonus is characterized by a moderate change in conductivity, mentioned above, and a profound change in irritability. The irritability of the nerve is increased in the region of the kathode and decreased in the region of the anode. In Fig. 55 the line *A B* may serve for both nerve and abscissa. The curve *I–I′* indicates the degree of irritability; note that the irritability is increased in the region of the kathode and decreased in the region of the anode. It indicates also that the influence of the two electrodes decreases as the distance from the pole increases; and that in the intra-polar region there is a neutral area where the irritability is neither increased nor de-

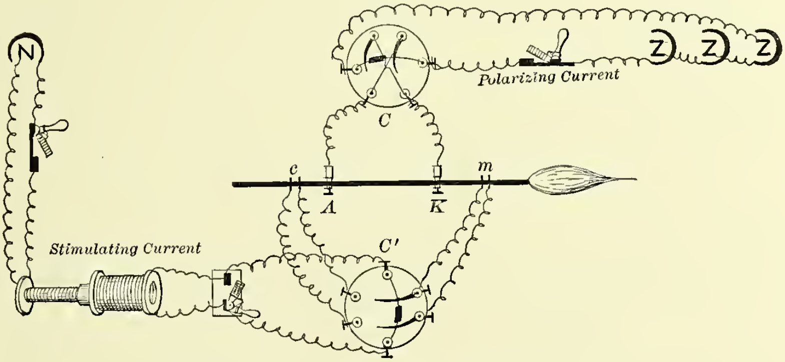
Fig. 55.



Digram illustrating electrotonus. *N.-P.E.*, non-polarizable electrodes; *An.*, anode; *Kt.*, kathode; *I,I′*, curve illustrating degree of irritability—decreased in the region of the anode and increased in the region of the kathode.

creased. The region of decreased irritability in the neighborhood of the anode is said to be in a condition of *anelectrotonus*; the region of increased irritability in the neighborhood of the kathode is said to be in a condition of *katelectrotonus*. The change in irritability manifests itself when a stimulus is applied to the nerve in the region of anelectrotonus or of katelectrotonus. Arrange the apparatus as indicated in the diagram (Fig. 56). Through the agency of commutator C one can make either electrode the kathode by reversing the current. Through commutator C' one can throw the stimulus at m, the muscular end of the nerve, or at c, the central end of the nerve. Arrange the apparatus so that the kathode is near the muscle as indicated in the figure. Before "making" the constant or "polarizing" current stimulate with the induced current at m or c, using a "break-shock" that will cause a moderate contraction, *i. e.*, bring the secondary coil just inside the minimum limit of stimulation. Turn on the polarizing current after a few moments, stimulate at m, in the katelectrotonic region; the response will be noticeably greater than the normal. Stimulate at c in the anelectrotonic region; the response will be noticeably less than the normal. Reverse the direction of the polarizing current bringing the anode nearer to the muscle. The region which before was in a condition of katelectrotonus is now in a condition of anelectrotonus and conversely. Stimulate in the region m and the response will now be less than normal because the irritability of the nerve has been decreased in the region of the anode, in the region of anelectrotonus. On the other hand the response at c will be greater than normal because of the influence of the kathode, inducing a state of katelectrotonus. These facts are summed up in a law of electrotonus:

FIG. 56.



Arrangement of apparatus for demonstrating electrotonus.

LAW IV. *The passage of a constant current through a nerve* *modifies its irritability, increasing it in the region of the kathode* (state of katelectrotonus) *and decreasing it in the region of the anode* (state of anelectrotonus).

d. Pflüger's Law of Contraction.

If one stimulate the nerve of a muscle-nerve preparation, and note visually or graphically the response which the muscle gives he will find that with uniform and favorable conditions the preparation will respond in a uniform way to a varying stimulus. The stimulus should be varied in two ways: (I) as to direction; (II) as to strength. If the current pass along the nerve toward the muscle, *i. e.*, the kathode being placed nearer to the muscle the current is called a "*descending*" one; if the anode is nearer to the muscle the current is called an "*ascending*" one.

To vary the strength of the current one should use either a simple rheocord or a DuBois-Reymond rheocord, so that the strength may be varied by infinitesimal increments. Non-polarizable electrodes are preferable, though platinum electrodes may be used with good results. Choose healthy, vigorous frogs; pith them two or three hours before they are to be used. Protect the preparation against rapid drying by mounting it in a moist chamber. With all conditions favorable the results will be as follows: A very weak ascending current will affect the muscle first, causing a slight contraction on *make.* With a somewhat stronger current there will be a contraction *on make of both ascending and descending currents.* A further increase in the strength of current will call forth a response *on both make and break of both ascending and descending current.* As the current is gradually increased from this point it will be noted that the contractions are not equal in extent; some are stronger and some are weaker; the weaker ones finally drop out and the stronger ones increase in strength. These strong contractions occur *on the make of the descending current and on the break of the ascending current.* The results may be thus tabulated:

CURRENT.	DESCENDING.		ASCENDING.	
	MAKE.	BREAK.	MAKE.	BREAK.
Weak.	Contract.	Rest.	Contract.	Rest.
Medium.	C	C	C	C
Strong.	C	R	R	C

It now becomes necessary to account for these results using the laws which have been formulated. To that end let us here present the laws again.

Law I. *The make stimulus is kathodic; the break stimulus is anodic.*

Law II. *The make or kathodic stimulus of a current is more irritating to nerve or muscle than the break or anodic stimulus.*

Law III. *A strong constant current decreases the conductivity of a nerve in the region of the anode during the passage of the current and in the region of the kathode after removal of the current.*

Law IV. *The passage of a constant current through a nerve modifies its irritability, increasing it in the region of the kathode* (state of katelectrotonus) *and decreasing it in the region of the anode* (state of anelectrotonus).

The results tabulated above may be graphically represented as shown in the accompanying figure (Fig. 57).

Fig. 57.

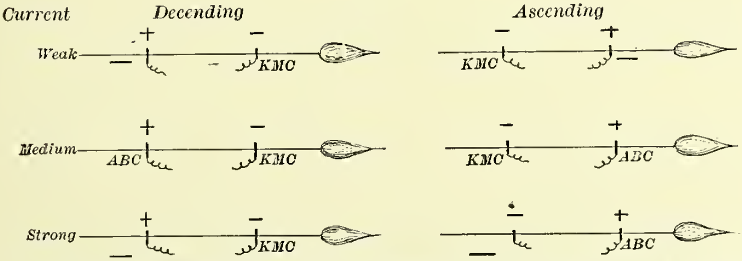


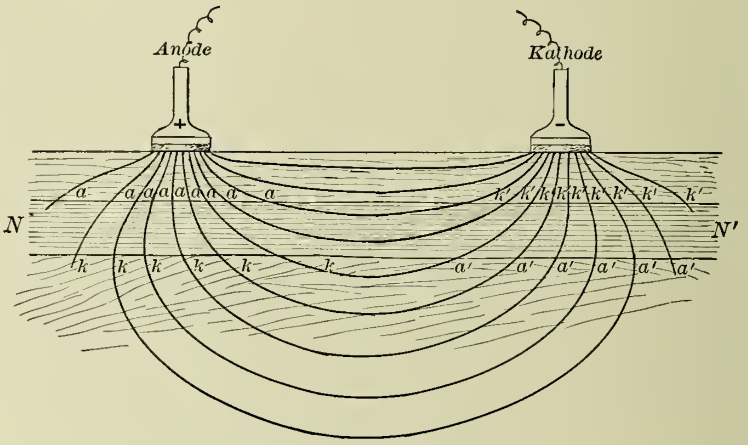
Diagram showing schematically the results of Pflüger's law of contraction. *KMC*, kathodic make contraction; *ABC*, anodic break contraction.

Note that with a weak descending current there is a "kathodic make contraction" (*KMC*); that with a medium descending current there is both an "anodic break contraction" (*ABC*) and a "kathodic make contraction" (*KMC*). The other indicated results will be found to correspond to the table. Why is there a kathodic make contraction only, with a weak descending current? Because (I) the make contraction starts at the kathode (Law I.); (II) there will be a kathodic contraction before there is an anodic contraction in accordance with law II. These laws account also for the results obtained with an ascending current. With a medium current, kathodic make contraction is in response to law I. The fact that there is an anodic break contraction indicates that in response to law II. the break stimulus has become sufficiently strong to cause a response. The same thing is true for both ascending and descending currents. In the case of a strong descending current we get a kathodic make contraction in response to law I. In response to an anodic break stimulus there is no contraction because according to law III. the conductivity is decreased in the region of the kathode at the moment of the break of a strong current. At the make of a strong ascending current there is no response though there has been a strong kathodic stimulus because the conductivity of the nerve is much decreased in the region of the anode *during* the passage of the strong current (Law III.). In this case the anodic break stimulus causes a contraction because the region of reduced kathodic conductivity is not between the stimulated point and the muscle.

e. The Application of the Laws of Electrotonus.

In the application of the laws of electrotonus to the problems of electro-diagnosis or electro-therapeutics there are some complicating factors to consider. If the electrodes (usually metallic plates covered with chamois or sponge which is moistened when in use) are placed over the course of a nerve the current will diffuse widely through the tissues from the anode and converge again upon the kathode on leaving the tissues (see Fig. 58). Let $N N'$ represent a nerve trunk, the current enters it at a a a a traversing it and leaving by k k k. As the current converges toward the kathode it traverses the nerve trunk again entering at a' a' a' and leaving at k' k' k'.

Fig. 58.



Application of the laws of electrotonus.

But the point where a current enters a nerve is called the anode and the point where it leaves the kathode. This leads to the differentiation of four physiological poles while there are only two physical poles.

(I) The physiological anode under the physical anode; (a, a, etc.).

(II) The physiological kathode under the physical anode; (k, k, etc.).

(III) The physiological anode under the physical kathode; (a', a', etc.).

(IV) The physiological kathode under the physical kathode; (k', k', etc.).

A contraction caused by the influence of the current at the physiological kathode under the physical anode is called an anodic make contraction (*AMC*). A contraction caused by the influence of the current at the physiological anode under the physical anode is called anodic break contraction (*ABC*). In a similar way there may be a kathodic make contraction (*KMC*), and a kathodic break contraction (*KBC*).

It is important to determine which of these various stimuli will be most effective. In addition to the above laws of electrotonus one will need to apply a fifth law.

Law V. *The denser the current, all other things being equal, the stronger the stimulus.* In the figure note that the current is denser at the physiological anode under the physical anode than at the physiological kathode under the physical anode.

The kathodic make contraction is stronger than the anodic break contraction.

(1) .... $KMC > ABC$.

This is in accordance with laws I. and II., law V. not applying here because the density is the same, providing the nerve is equally near the surface under the two poles. For similar reasons, *the anodic make contraction is stronger than the kathodic break contraction.*

(2) .... $AMC > KBC$.

If *KMC* is greater than *ABC* and if *AMC* is greater than *KBC* we may conclude that:

(3) .... $KMC + AMC > ABC + KBC$ or *the sum of the make stimuli must be greater than the sum of the break stimuli,* in consequence of this, *the contraction which occurs at make* (in response to the double stimulus), *is greater than the contraction which occurs at break* (in response to the double stimulus).

The anodic make contraction (*AMC*) *may or may not be stronger than the anodic break contraction* (*ABC*), *i. e.,*

(4) .... $AMC > ABC$ or $AMC < ABC$.

In this case we have the stronger effect at the physiological kathode (Law I.) to offset the greater density of the current at the physiological anode (Law V.) one may be stronger than the other, but the difference is at most slight.

We are now in a position to understand what will take place when the current is progressively increased from weak to strong. The results may be thus tabulated:

Weak Current	*KMC*			
Medium Current	*KMC*	*AMC*	*ABC*	
Strong Current	*KMC*	*AMC*	*ABC*	*KBC*

The above table gives the normal reaction. *If degeneration has made some progress the weak current elicits the anodic make contraction (AMC) before it does the kathodic make contraction (KMC)*, an important fact in electro-diagnosis.

B. THE GENERAL STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM.[1]

We have studied the way in which contractile and irritable tissues respond to certain external and artificial stimuli. Before we enter upon the special physiology of the various organs and systems of organs it will be profitable for us to briefly consider: (I) what relation nervous tissue bears to the organism as a whole; (II) whence come the various stimuli which influence the operation of the different organs and tissues of the body; (III) what tissues (besides contractile tissues) are influenced in their activity by the central nervous system.

1. GENERAL CONSTRUCTION OF THE NERVOUS SYSTEM AND ITS RELATION TO THE ORGANISM AS A WHOLE.

Though the tissue of the nervous system is disposed in prominent structures which may be called organs, *e. g.*, brain, spinal cord, etc., these structures are not organs in the same sense that the lungs are organs belonging to the respiratory system. *The whole nervous system is really one organ.* This organ is composed of (I) a parenchymal tissue, which is the specialized tissue of the organ, endowed with a specialized function; and (II) a supporting tissue. As in other organs, so here the supporting tissue belongs to the connective tissue series, the more delicate connective tissue of the deep-lying portions of the central nervous system being somewhat specialized and called neuroglia, while the remainder represents the more common forms of areolar, fibrous and elastic connective tissues.

a. The Neuron.

The parenchymous or active tissue of the nervous system is composed of nerve cells. The nerve cell is so highly specialized

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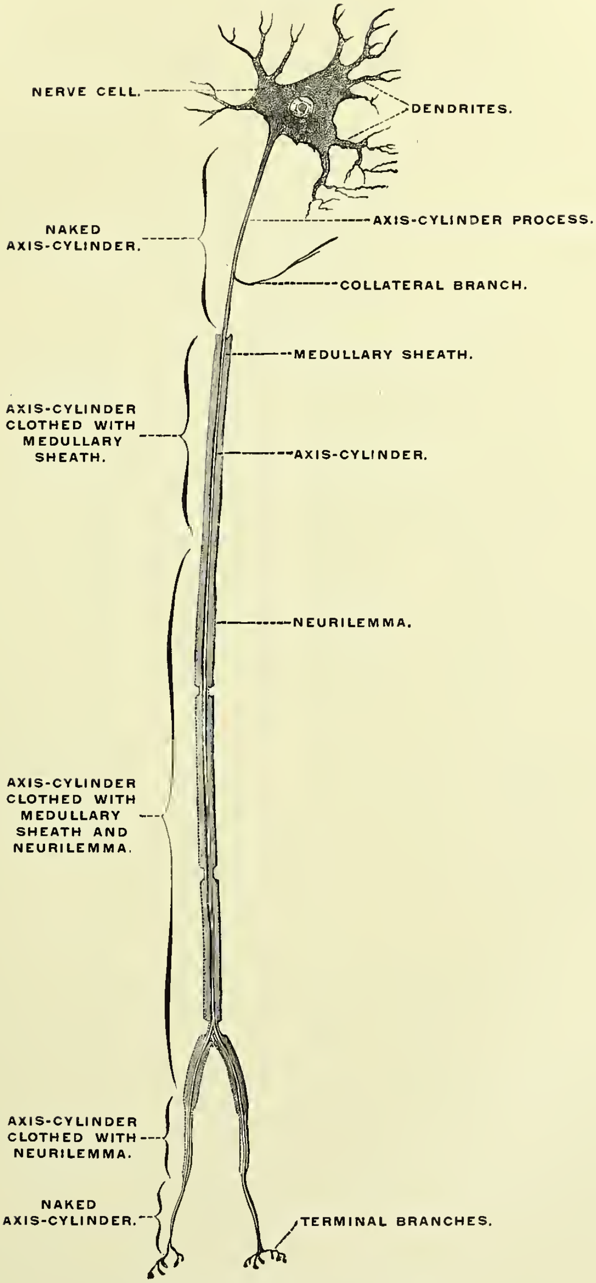
[1] The student is not in a position to comprehend the way in which the various systems of organs and tissues (circulatory system, respiratory system, digestive system, etc.) are governed; how they are influenced by outside conditions, and how one system exerts an influence upon another, unless he has at least a general idea of the construction of the nervous system and the functions of its various structures. It is the object of this section to give a brief outline of the most essential features of the nervous system.

FIG. 59.



Schema of a neuron. (After VERWORN.)

a structure that it has received the special name *Neuron.* The neuron is the unit of structure of the nervous system. *A neuron* (see Fig. 59) *consists of a neural cell-body with all of its processes.*

The protoplasm of the cell body presents a delicate fibrillated structure. The fibrillæ seem to be continuous with those which constitute the one or two axis-cylinders which are among the cell processes. Besides the fibrils, the cell protoplasm is more or less charged with fine dark granules, which are important in the metabolism of the cell, increasing during periods of rest and decreasing during periods of activity. Occupying a fairly central position in the cell-body is a relatively large nucleus, with a distinct nucleolus (plasmosome).

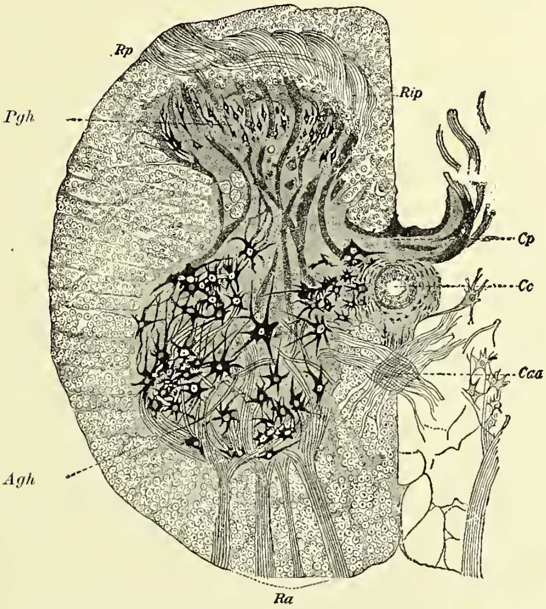
The cell-processes are numerous and complex. As to structure they may be arranged in two classes: (I) The protoplasmic process,—short and much branched, their tree-like appearance giving them the name *Dendrites.* (II) The axis-cylinder process, which is usually much elongated, little branched near the cell-body and usually insulated in a medullary sheath. As to function, cell-processes either bring impulses to the cell-body or they carry impulses away from it. Those which bring impulses to the cell-body are called *afferent* cell-processes and those which carry impulses away are called *efferent* processes. The protoplasmic processes are without exception afferent.

If a cell has only one axis-cylinder it is without exception efferent. If it has two, one of them is afferent and one efferent. These facts readily lead to confusion in the use of terms. To avoid this confusion the best authorities are now adopting a new term to represent the efferent process—the term NEURAXON or *Neurite,* or *Axon.* As now understood *the term dendrite always refers to an afferent process. All neuraxons are axis-cylinders structurally.* Most dentrites are protoplasmic processes, but some (the sensory nerves) have become modified into axis-cylinders.

b. Features of the Spinal Cord.

The nerve trunks with which one deals in the experiments in muscle-nerve physiology are really bundles of insulated neuraxons. They normally carry motor impulses to the muscles from the cell-body which they represent. But where is this cell-body located? If one follow the nerve trunk he will find that just before reaching the central system it divides into two roots, an anterior (or ventral) root and a posterior (or dorsal) root. If the anterior root be stimulated one will observe the same response as if the trunk had been stimulated in the same way nearer to the muscle. If the posterior root be stimulated no such response will be observed.[1] One is justified in inferring that the neuraxons which he is tracing left the spinal cord by the anterior roots. A transverse section of the spinal cord should show the large cell-bodies in the anterior gray horn (see Fig. 60). Note their numerous branches. In a few cases the neuraxons may be traced into the nerve bundles which make up the anterior root. From the accompanying diagram note that the motor neuron in question is in communication—through its dendrites: (I) with motor neurons from the brain and (II) with sensory neurons. (See Fig. 61.)

FIG. 60.



Half of a section through the lumbar cord. *Ra*, anterior root; *Rp*, posterior root; *Rip*, inner portion of the posterior root; *Cp*, posterior commissure; *Caa*, anterior commissure; *Cc*, central canal. The fine net-work of medullary fibers in the gray matter and the net-work of medullary fasciculi in the otherwise gray posterior commissure are not shown. *Agh*, anterior gray horn; *Pgh*, posterior gray horn. (EDINGER after DEITERS.)

The motor neuron normally sends a motor impulse to the muscle which it supplies, only when it receives an impulse through its dendrites. From the connection which it has it is evident that it may receive such an impulse from one or the other of two sources: (I) from the brain; (II) from the sensory system of nerves. If the motor impulse originates in the brain it is sent through the central motor neuron to the peripheral motor neuron, thence through it to the muscle. Two neurons, two cells, are re-

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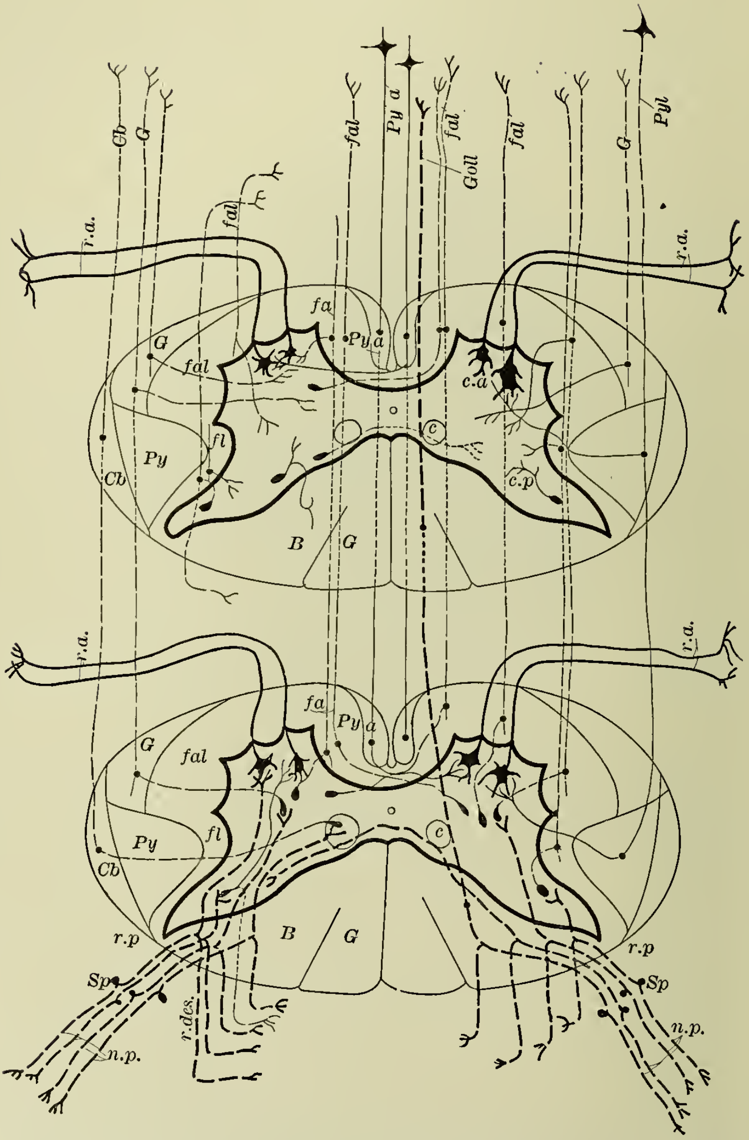
[1] There may be a general response, the nature of which will be explained later; but there will be no definite response of the particular muscles supplied by the motor nerve in question.

FIG. 61.



Schematic representation of the course of the fibers in the spinal cord. (WHITAKER.) I. *The Motor Tract.* *a.* Central neuron: Lateral pyramidal tract (*Py l*) and anterior pyramidal tract (*Py a*); terminal arborization in the anterior horn. *b.* Peripheral neuron: anterior horn cells—anterior root (*r. a*)—motor nerve muscle. II. *The Sensory Tract.* *a.* Peripheral neuron: sensory nerve (*n. p*), spinal ganglion (*Sp*)—posterior root (*r. p*) of the spinal cord. In the posterior root zone of the posterior columns each fiber divides into an ascending and a descending branch (short and long fibers). The short tracts curve into the posterior horn as: 1. Reflex collaterals to the anterior horn, shorter reflex arc, longer reflex tracts (intercalation of another neuron). 2. Fibers to the cells of the middle zone of the gray substance. 3. Fibers to the cells of Clarke's columns (*c*). 4. Fibers to the central and especially the medial anterior horn cells (commissural cells). 5. Fibers to the posterior horn cells. The long tracts (6) pass first into Burdach's column, higher also into Goll's column, and thus to the nuclei of the posterior columns in the medulla. (Here they join the fillet.) *b.* Central neuron. It begins with the cells of the terminal places of the peripheral, enumerated under 2 to 6. 1. From those which have been enumerated under 2 as "column cells" arise the fibers of the anterior ground bundle of the same side (*fal*) (*fl*) and the columns of Gowers (*G*). 2. From those mentioned under 3: the lateral cerebellar tract of the same side (*Cb*). 3. From those under 4: fibers which cross in the anterior commissure to the anterior lateral column (*fal*) (*fl*) to ascend in the other side. 4. From those under 5: fibers to the lateral limiting layer (*fl*) and to the ventral field of the posterior columns. In addition to this is represented the manner in which the collaterals are given off and the termination of the central short tracts (which quickly bend again into the gray substance) of the anterior lateral columns, the "inland cells" (Golgi) in the posterior horn; the decussation in the posterior commissure is not clear. There are contained in the posterior roots apparently other individual fibers which have their neuron cells in the anterior horn, but in man this is not yet satisfactorily established.

quired to transmit an impulse from the brain to the peripheral organs. This holds good for secreting and excreting organs as well as for motor organs. But the peripheral motor neuron may be influenced by sensory neurons, by neurons which bring impulses to the central nervous system from the skin and various sensitive organs of the periphery. Note in the diagram that these peripheral sensory neurons (sensory neurons of the first order) enter the spinal cord by the posterior root, and that they communicate (I) either directly or indirectly with a motor neuron; (II) either directly or indirectly with the brain. Note that a spinal ganglion (*Sp*) is located upon the posterior root. This ganglion of the posterior root is the location of the cell-bodies of the peripheral sensory neurons. From the peripheral sense organ to the cell-body in question the impulse is conducted along an afferent axis-cylinder which is a modified dendrite. From the cell-body the impulse is conducted into the spinal cord along an efferent axis-cylinder or neuraxon. This neuraxon sends off collateral branches which communicate directly with peripheral motor neurons, of the same segment, or indirectly with motor neurons of neighboring segments of the cord, or finally directly or indirectly with the brain through a central sensory neuron (or neuron of the second order).

2. GENERAL FUNCTIONS OF THE NERVOUS SYSTEM.

a. Reflex Action.

A careful study of these relations between the sensory and motor neurons makes it evident that the activity of any peripheral motor (or glandular) organ may be influenced in one or the other of two ways: (I) through the direct influence of impulses entering the central system by the sensory neurons of the same (or neighboring) segment which furnishes the motor nerve supply; or (II) through the influence of the brain. The first method of influencing the activity of an organ is called reflex. Note that reflex action involves typically two neurons: the peripheral sensory neuron and the peripheral motor neuron. Reflex response to a stimulus, as when one jerks his hand from a hot object, is accomplished in the following manner: (I) The sensory nerve endings in the skin are stimulated by the hot object; (II) The stimulus starts a message or impulse along the afferent nerve to the cell-body in the posterior root ganglion; (III) The cell receives the impulse and transmits it along the efferent neuraxon to neighboring motor neurons (and to the brain); (IV) The motor neurons respond to this stimulus by causing in certain muscles of the arm the contractions necessary to remove the hand from the painful object.

b. Voluntary Action.

In the meantime the sensory impulse has been transmitted to the brain and the individual becomes conscious not only that his hand has suffered an injury but that a reflex act has occurred through which the hand has been removed from the immediate danger. The consciousness of injury aroused in the brain may be the stimulus to further acts on the part of the organism toward further protection or toward repair of injury already done. These secondary and conscious acts of adaptation cannot be classified as reflex; they are voluntary acts, suggested by the brain, which in turn is actuated by the stimulus described above, possibly also by visual and other supplementary stimuli.

c. Nerve Centers.

1. **Centers in the Spinal Cord.**—In describing reflex action each segment of the cord has been described as a center toward which afferent impulses come, and from which efferent responsive impulses are sent out. Each segment of the spinal cord is thus a *motor center* for a limited number of muscles. But there are other centers in the spinal cord. There are centers which preside over: (I) the nutrition of tissues: *i. e., trophic centers* to muscles, nerves, bones, joints; (II) walls of blood vessels; *i. e., vaso-dilators;* (III) secretion of skin—sweat centers; (IV) centers connected with *micturition, erection of the penis, parturition,* and *defecation.*

The motor, trophic, and vaso-dilator centers are distributed along the whole extent of the spinal cord; but the centers enumerated under (IV) are probably located in the lumbar enlargement of the cord.

2. **Centers in the Medulla Oblongata.**—In the spinal bulb, or medulla oblongata, there are numerous reflex centers, whose action will be discussed later:

(I) *Respiratory;* (II) *Vasomotor;* (III) *Cardiac centers;* (IV) also centers for *coughing, sneezing, mastication, deglutition, vomiting, coördinating, convulsor, closure of eyes, dilation of pupil, salivary, sudorific, diabetic,* etc. Most of these centers are located in the floor of the fourth ventricle.

3. **Nerve Centers in the Brain.**—(*a*) THE CEREBELLUM contains the following centers: (I) Centers for the *coördination* of *movements;* (II) *Emotional Centers;* (III) *Centers for Muscle Tonus.*

(*b*) THE CEREBRUM contains the following centers: (I) Smell; (II) Taste; (III) Hearing; (IV) Vision; (V) Speech; (VI) Various motor centers; (VII) Thermogenic centers.

PART II.

SPECIAL PHYSIOLOGY.

Division A. NUTRITION.
THE PHYSIOLOGY OF THE INTERNAL RELATIONS.
Division B. MOTO-SENSORY ACTIVITIES.
THE PHYSIOLOGY OF THE EXTERNAL RELATIONS.
Division C. REPRODUCTION.

DIVISION *A.*

NUTRITION.

Chapter III. CIRCULATION.
Chapter IV. RESPIRATION.
Chapter V. DIGESTION.
Chapter VI. ABSORPTION.
Chapter VII. METABOLISM.
Chapter VIII. EXCRETION.

NUTRITION.

INTRODUCTION.

The general term *Nutrition* is applied in Physiology to all of those activities, collectively taken, which are involved in supplying the cells of the body with food, in building this food up into cell substance, in liberating the energy from it by katabolic processes and in ridding the body of the waste material, which results from those processes.

A general idea of the activities and organs involved in nutrition may be gained from the following table :

Activities.		Organs or Tissues.
1. Perception.		Organs of the Special Senses.
2. *Prehension.*		Hands, Teeth, etc.
3. Preparation.		Hands, etc.
4. *Mastication.*		Teeth.
5. Deglutition.		Invol. Muscles of Pharynx and Œsophagus.
6. DIGESTION.		Secretory Apparatus : Gastric Glands, Liver, Pancreas, Intestinal Glands.
7. ABSORPTION.		Epithelium of Alimentary Canal.
8. CIRCULATION.		Blood and Lymph Circulatory Systems.
9. Selection.		Individual Cells of the body.
10. METABOLISM.	I. ANABOLISM.	Individual Cells of the body.
	II. KATABOLISM.	Individual Cells of the body.
11. RESPIRATION.	I. *External* R. [*Circulation* (*b*)]	Lungs, Air Passages, Muscles of Respiration.
	II. Internal R.	Individual Cells of the Body.
12. Rejection of waste products from the [*Circulation* (*c*)]		Cells of the body.
13. EXCRETION.	I. Renal	Kidneys.
	II. *Pulmonary*	Lungs.
	III. *Cutaneous*	Sweat-glands.
	IV. *Hepatic*	Liver.
14. EGESTION.	1. *Micturition*	Bladder, etc.
	2. *Expiration.*	Air passages.
	3. *Perspiration*	Skin.
	4. *Defecation*	Rectum.

To illustrate the table we may follow the steps of a cat's nutrition : (I) Through the organs of scent and sight she perceives her prey. (II) With claws and teeth the *prehension* or catching is accomplished. (III) The *preparation* is in this case a simple killing, but man prepares his food usually by cooking. (IV) She *masticates* it ; (V) swallows it ; (VI) *digests* it. (VII) The digested portion is *absorbed ;* passes through the *circulation,* (VIII) to the cells of the body, where each cell selects (IX) an appropriate part, which it builds up (X′) into cell substance. After a time the cell protoplasm is broken down (X″) incidental to the functional activity of the cell ; the balance of chemical affinity is immediately restored by the introduction into the cell of the oxygen (XI″) which has been brought from the *lungs* (XI′) by the *circulatory* system. The products of katabolism are promptly *rejected* (XII) from the cell, carried to the periphery by the circulation where they are *excreted* (XIII) by the proper organs and finally *ejected* (XIV) from the body.

After a moment's reflection it will be seen that—either directly or indirectly—*every organ* and *every function* of the *organism is brought into action in nutrition, except those of reproduction.*

Inasmuch as the circulatory system is variously and repeatedly involved in nutrition it will be more advantageous to treat that first than to interrupt the course of the discussion after the subject of digestion is opened. Respiration being a collateral branch of nutrition, a similar course may profitably be pursued regarding it. With an understanding of the circulation and respiration at command we may enter upon the uninterrupted discussion of digestion; absorption ; metabolism ; and excretion.

CHAPTER III.

CIRCULATION: INTRODUCTION.

A. THE COMPARATIVE PHYSIOLOGY OF THE CIRCULATION.

1. THE CIRCULATING FLUIDS.
2. THE ORGANS WHICH CAUSE THE CIRCULATION.

B. ANATOMICAL INTRODUCTION.

1. THE BLOOD-VASCULAR SYSTEM.
2. THE LYMPHATIC SYSTEM.
3. THE SPLEEN.
4. HISTOGENESIS OF THE CIRCULATORY ORGANS AND TISSUES.

C. PHYSICAL INTRODUCTION.

1. THE FLOW OF LIQUIDS THROUGH TUBES.
2. MANOMETERS.

D. HISTORICAL INTRODUCTION.

INTRODUCTION.

As soon as an animal attains to the dignity of an individual of the third order (See Individualization of Living Matter, Gen. Physiol., Part I.); *i. e.*, as soon as it has more than an ectoderm and entoderm the necessity arises of conveying to the middle layer or mesoblast the nourishment obtained from the environment by the layers which lie in immediate contact with the environment. And thus the circulatory system is born of necessity. It is a system of tubes taking up fluid or gaseous food from the hypoblast and conveying it to all parts of the body. This system of tubes, filled with a fluid kept in circulation through the agency of the heart, has fine ramifications in all parts of the body, and serves not alone to carry nourishment, but also to remove the waste material from the active cells. Further, the blood serves as a distributor of warmth and moisture in the body.

A. THE COMPARATIVE PHYSIOLOGY OF THE CIRCULATION.

The primary object of the circulation is the distribution of nutriment to tissues which do not lie in or adjacent to absorbing surfaces. Secondarily the fluids in circulation carry oxygen from the absorbing surfaces to the other active tissues, and finally these fluids carry to the periphery of the organism for excretion certain waste products which are of no further use to the system. As a "common carrier" the circulatory system is the servant of the fundamental process of nutrition. In each one of its various capacities it seems to be essential to the organism.

In the description of this system it is convenient to treat (I) the circulating fluids, and (II) the organs which cause the circulation of the fluids.

1. THE CIRCULATING FLUIDS.

(*a*) THE MOST PRIMITIVE CONDITION is represented by the *cœlenterates* whose *gastrovascular* system of canals is filled with a fluid which is composed of the digested or partly digested ingesta and of imbibed water. This fluid may be called a *circulating chyme.* It is devoid of corpuscular elements. The oxygen which it holds in solution may be absorbed by the cells which are adjacent to the canals, but it lacks any special agent to serve as an oxygen carrier.

(*b*) NEXT IN ORDER as a circulating fluid may be considered the *circulating chyle* or hydrolymph of *echinoderms, lamellibranchiate molluscs, tunicates* and the *amphioxus.* This fluid differs from the circulating chyme in having passed into the organism through an absorbent surface of epithelium. It is a selected fluid and, therefore, much more uniform in its composition than is the crude circulating chyme. This circulating chyle is corpusculated. The corpuscles are not particularly abundant and are similar to the lymph corpuscles and leucocytes of higher vertebrates,—being capable of amœboid movements and varying much in size.

(*c*) THE TERM *hæmolymph* is applied to the circulating fluid possessed by *worms,* most *molluscs,* and *arthropods.* Hæmolymph is distinguished from hydrolymph in having *hæmoglobin* or other oxygen-carrier *in solution.*

(*d*) THE MOST COMPLETE SYSTEM of circulating fluids is possessed by the vertebrates (amphioxus excepted). The circulating chyle is received into the lymphatic system of vessels and mixed with true lymph. This soon mixes with the blood,—the most complex of all circulating fluids. The blood of vertebrates consists of (α) a fluid-plasma, quite like the fluid portion or plasma of the lymph, (β) corpuscular elements which in turn are: (I) the leucocytes which are practically the same as the lymph corpuscles, (II) the red corpuscles which are characteristic of the vertebrates, though they have been also observed in a few isolated invertebrate genera. The essential feature of the red blood-corpuscle is *Hæmoglobin.*

The hæmolymph contains various oxygen-carriers, or respiratory pigments (hæmoglobin, hæmerythrin, hæmocyanin), in solution, while *the blood contains hæmoglobin in corpuscular form.* These hæmoglobin corpuscles are retained within a definite system of canals, the *blood-vascular* system; while the lymph circulates in a vaso-lacunar system similar to that possessed by most of the invertebrates. Note (I) that in the *circulating chyme* the sole function of the fluid is to carry nutriment; (II) that the hydrolymph carries nutriment to the tissues and excrement from them; (III) that the hæmolymph carries *nutriment and oxygen* to the tissues and excrement from them; (IV) that in the blood-lymph systems the same functions are performed, but there is a differentiation of structure and composition between blood and lymph and the functions are performed more perfectly because of this specialization.

2. THE ORGANS WHICH CAUSE THE CIRCULATION.

(*a*) THE CŒLENTERATES have a system of canals which are really diverticula from the gastric cavity. The fluid within this *gastro-vascular* system of *canals* is set in motion by the general movements of the animal.

(*b*) THE LOWEST ORDER of circulatory system is that in which the hydrolymph and hæmolymph of the invertebrates flow. As a general rule the lymph is kept in motion by the rhythmical contractions of some portion or portions of the canal system. These pumping organs are called *hearts.* The animal kingdom presents hearts of various forms and degrees of complexity, but they all have this in common that they represent dilatations of the blood vessels. In Mollusca and Arthropoda the heart is located dorsally, in Vertebrates it is ventral. There are two general methods of propulsion: (I) *Peristalsis.* The earthworm possesses a series of segmental arterial arches connecting the ventral and dorsal trunks. The rhythmic peristalsis of these arches keeps the blood (hæmolymph) in circulation. The amphioxus has a similar system physiologically; the contractile portions are upon the ventral vein forcing the lymph to the branchial system (respiratory heart) and upon the dorsal artery, forcing the lymph through the systemic capillaries (systemic heart). (II) *Pumping.* The second method of propulsion is by a force-pumping mechanism, the essential features of which are the strong muscular walls, the valves, and the filling chambers. The first of these insures a comparatively quick and strong contraction of the walls of the heart upon the fluid contents, but the pressure (intra-ventricular) is equally distributed over the walls of the organ and the fluid is as likely to go back through the way by which it entered as to go forward unless it be blocked. The valves at the entrance of the heart stop this regurgitation and insure the forward movement of the circulating fluid. To be mechanically effective the heart must fill quickly. This necessity is satisfied in arthropoda by a filling chamber around the heart—the pericardium—into which the blood flows during cardiac contraction. When the heart relaxes the collected lymph quickly enters its cavity through the open valves. A similar function is performed by the auricles of the mollusks.

In most invertebrates the blood escapes into tissue spaces at the end of its arterial flow.

After traversing the tissue spaces and LACUNÆ the lymph makes its way into the vessels which return it to the organ of propulsion. The lacunæ and tissue spaces of invertebrates correspond to the lymph or serous cavities and lymph radicles of the higher animals.

(*c*) THE VERTEBRATES,—above Amphioxus,—possess the highest type of circulatory system—the blood is propelled by a heart fully equipped with valves and filling chambers. The Amphioxus has two hearts,—respiratory and systemic. Fishes have a respiratory heart whose strength is sufficient to carry the blood through the systemic vessels after it has been aërated.

In the Amphibia and lower Reptiles there are two auricles but only one ventricle which must serve both as respiratory and systemic heart. In these animals there is, to a certain extent, a mixture of the aërated and unaërated blood. The devices for insuring the purer blood current for the cephalic end of the animal are to say the least ingenious. In crocodiles, birds and mammals the heart is double, each half being composed of an auricle and a ventricle. The right half of the heart is the respiratory heart and the left side the systemic heart.

The morphological details by which these various points are accomplished are matter for anatomy rather than for physiology.

B. ANATOMICAL INTRODUCTION.

1. THE BLOOD-VASCULAR SYSTEM.

Structural features of the heart and vessels which are of special physiological importance.

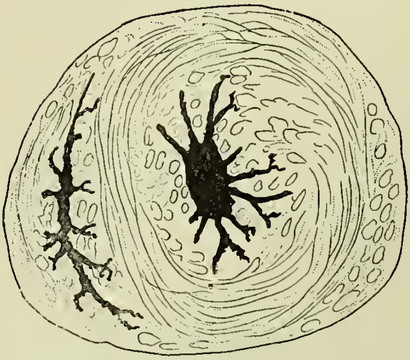
a. The Heart.

1. **The Musculature.**—(*α*) Several muscle layers; longitudinal, oblique and circular, so intricately arranged that one system of fibers may often be traced in all of the directions in turn.

(*β*) Many fibers or bundles arise from the auriculo-ventricular ring, and after making their circuit, return again to an opposite segment of the ring.

(γ) Some bundles arise from the ring, make their winding circuit and terminate in a papillary muscle.

Fig. 62.



Cross-section through a completely contracted human heart, at the junction of the middle and lower thirds. (Krehl.)

(δ) The bases of the aorta and pulmonary arteries are surrounded by circular heart fibers, and further, many of the longitudinal fibers arise from the region of the great vessels.

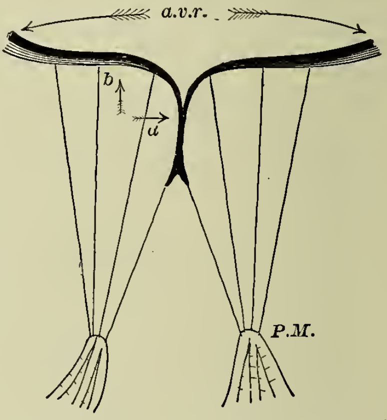
(ε) The musculature of the left ventricle is very much heavier than that of the right. (Fig. 62.)

2. **The Valves.**—(α) From the auriculo-ventricular ring valves, convex on the auricular surface, project toward the center of the ring.

(β) Each cusp, or flap, is much thicker near its origin on the ring than near the free margin.

(γ) Each cusp is stayed or guyed, from the ventral side, by several tendonous cords which pass from the apex of a papillary muscle to different parts of the cusp. (see Fig. 63.)

Fig. 63.



After Krehl. Diagram showing the general arrangement of the auriclo-vent. valves. *a.v.r.*, auric-vent. ring. *a*, plane of tangency. *P. M.*, papillary muscles.

(δ) The cusps meet at *a*, not in a common tangent line, but in a common tangent plane.

3. **The Cavity of the Heart.**—(α) The dilated cavity of the left ventricle is an inverted oblique, quadrilateral pyramid, presenting irregularities of surface, due to columneæ carneæ and papillary muscles. Its volume in the adult male is about 180 c.c. (β) The contracted cavity of the left ventricle presents in the upper segment a quadrilateral outline, in the lower segment, a triangular outline. From the central cavity, which at the end of systole may be almost obliterated, numerous crevasses pass out into the wall of the ventricle. These crevasses represent spaces between the fleshy columns or papillary muscles. (Fig. 62.)

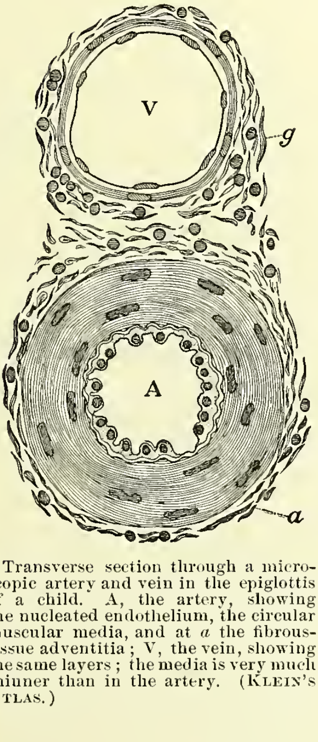
(γ) The dilated cavity of the right ventricle presents, on cross section, a crescentic outline. It is much shorter than the cavity of the left ventricle, though its volume is the same.

(*d*) The closed cavity of the right ventricle presents a series of irregular crevasses which together describe a crescentric field. (Fig. 62.)

b. The Blood Vessels.

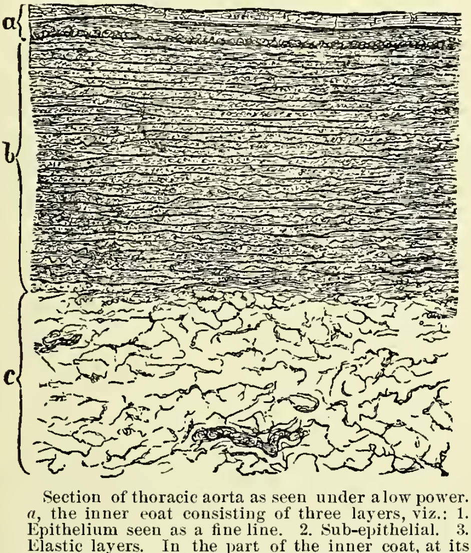
1. **The Arteries and Veins** are composed of practically the same elements in the same arrangement; the principal difference being the proportion of the different tissues entering into the composition of the several layers. The walls of the arteries are thicker, very much thicker. (Fig. 64.)

Fig. 64.



Transverse section through a microscopic artery and vein in the epiglottis of a child. A, the artery, showing the nucleated endothelium, the circular muscular media, and at *a* the fibrous-tissue adventitia; V, the vein, showing the same layers; the media is very much thinner than in the artery. (Klein's Atlas.)

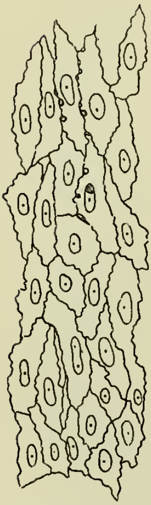
Fig. 65.



Section of thoracic aorta as seen under a low power. *a*, the inner coat consisting of three layers, viz.: 1. Epithelium seen as a fine line. 2. Sub-epithelial. 3. Elastic layers. In the part of the inner coat, at its junction with the middle, a layer of longitudinal muscular fibers is represented as cut across. *b*, middle coat with its elastic membrane; *c*, outer coat with two vasa vasorum. (Schaefer after Toldt.)

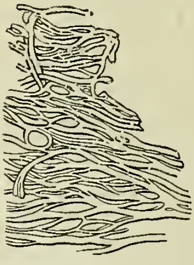
This is important for the following considerations: First, The greater thickness enables them to sustain the greater blood-pressure; Second, Their greater resistance enables them to withstand minor external pressure, *e. g.*, from muscular contraction or pressure of clothing, thus the parts supplied are subjected to a minimum accidental variation of blood-supply; Third, Their greater thickness makes them less vulnerable in accidents. The large arteries have relatively more elastic tissue, while the small arteries and arterioles have relatively more muscle-tissue. The reason is evident: The large vessels receive the direct impulse from the heart-beat. The heart can rest a part of the time. The walls of the arteries are under continuous, though varying strain. Muscle tissue alone could not long endure the strain of unremitting work ; only the unsensitive, unresponsive, elastic tissue can be safely put to so prodigious a strain. In the small arteries and arterioles the lateral pressure is very much less. The muscle fibers of these vessels, supplemented by a small amount of elastic tissue, are quite sufficient to sustain it. Further, the supply of blood to special organs is controlled by these muscle-fibers acting under the influence of the vaso-motor nerves. (See Figs. 65, 66.)

Fig. 66.



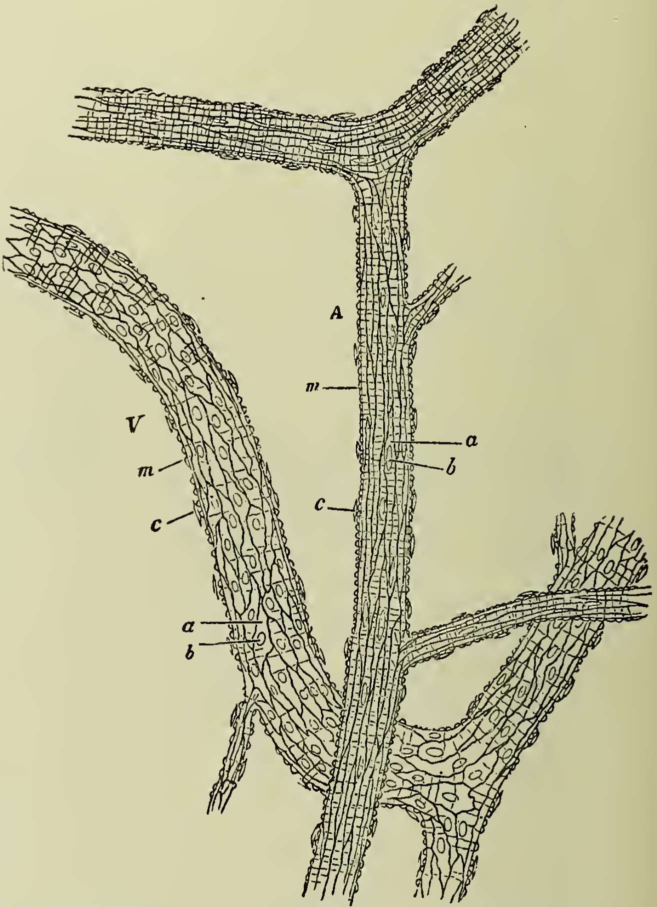
Epithelial layer lining the posterior tibial artery. (250 diameters.) (After Schaefer.)

Fig. 67.



Elastic network of artery. (Schaefer after Toldt.)

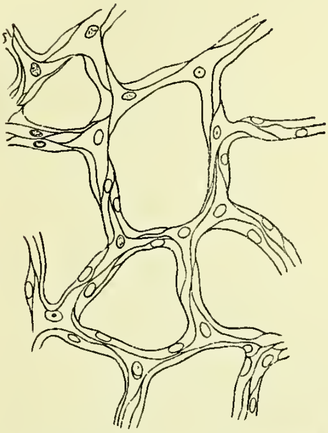
Fig. 68.



A small artery, A, and vein, V, from the subcutaneous connective tissue of the rat, treated with nitrate of silver. (175 diameters.) a, a, endothelial cells with b, b, their nuclei ; m, m, transverse markings due to staining of substance between the muscular fiber-cells ; c, c, nuclei of connective tissue corpuscles attached to exterior of vessel. (Schaefer.)

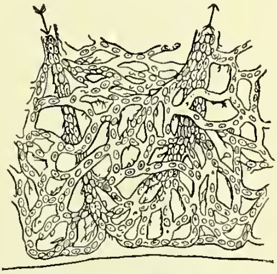
2. **The Capillaries.**—The capillary wall, consisting as it does of simple endothelial plates, can not withstand much pressure. Most of the energy exerted by the heart has been expended in overcoming the resistance between the heart and the capillaries so that the millions of capillaries are easily able to withstand the distributed remnant of pressure. Any increase of capillary pressure tends to increase the spaces between the endothelial plates and thus in turn to facilitate not only diapedesis of white blood corpuscles, but transudation of plasma. (See Figs. 69 and 70.)

Fig. 69.



Capillary vessels from the bladder of the cat, magnified. The outlines of the cells are stained by nitrate of silver. (Schaefer.)

Fig. 70.



Capillary blood vessels in the web of a frog's foot, as seen with the microscope. (A. Thomson.) The arrows indicate the course of the blood.

2. THE LYMPHATIC SYSTEM.

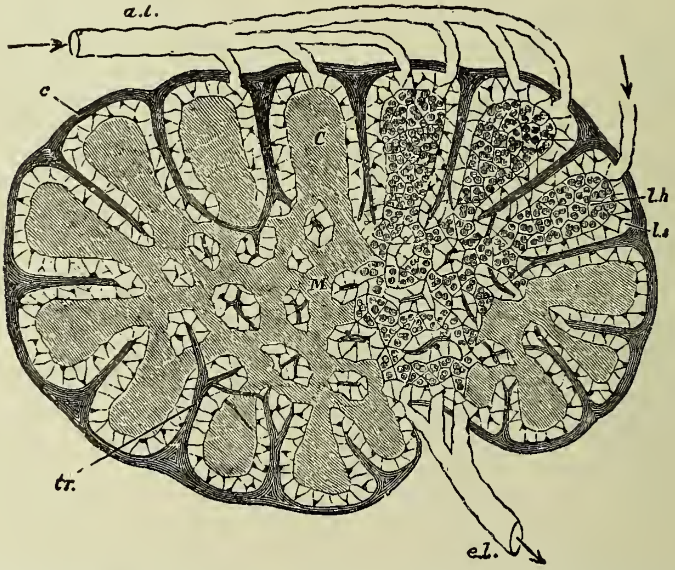
a. Lymphatic Follicles and Glands.

Lymphatic tissue is composed of two elements: 1st. A connective tissue reticulum associated with stellate connective tissue cells. This is called the *Adenoid Reticulum.* 2d. Small round cells which are enclosed within the meshes of the reticulum (Fig. 71). The lymphatic tissue, or adenoid tissue, is frequently found in small quantities along the arteries associated with the perivascular lymph channels; but it is usually collected in well-defined structures called lymph follicles.

1. **Lymph Follicles** are simple lymphatic nodules which occur in great numbers in the mucous membrane of the respiratory and alimentary tracts. Each follicle is surrounded by a delicate but close-meshed wall or capsule of fibrous connective tissue. Within this capsule the whole space is filled with typical lymphatic and adenoid tissue.

A lymph follicle receives its blood-supply from a vascular envelope composed of a loose meshwork of arterioles, from which capillary loops penetrate to the center of the follicles and return the venous blood to the corresponding meshwork of venules. Each follicle has an *afferent lymphatic*, which brings a stream of lymph which oozes through the adenoid tissue, and, emerging with fewer old leucocytes and more young ones, is carried off by the *efferent lymphatic.* Within the follicle old leucocytes which come laden with different materials, gathered in their wanderings, become helplessly entangled in the adenoid meshes and disintegrate. Within the follicle is a closely-packed group of leucocytes which are undergoing rapid reproduction by karyokinesis. Such a group of leucocytes is called a *Lymph Knot;* and this is the source of the young leucocytes which join the efferent stream. So the efferent stream from a lymph follicle or lymph gland may not contain more leucocytes than the afferent stream, but there will be more young active ones and fewer old sluggish ones. (Fig. 72.)

FIG. 71.



Diagrammatic section of the lymphatic glands. *a. l.*, afferent, *e. l.*, efferent lymphatics ; *C*, cortical substance ; *M*, reticulating cords of medullary substance ; *l. h.*, lymphoid tissue, *l. s.*, lymph-sinus; *c*, fibrous coat sending trabeculæ, *tr*, into the substance of the gland. (SCHAEFER.)

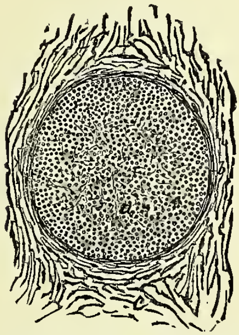
2. **A Lymph Gland** is simply a collection of lymph follicles. The structural variations are shown in Fig. 71. The functions are the same. The favorite locations of the lymphatic glands seem to be the *mesentery*, the groin, the axilla and the neck; though they are very generally but sparsely distributed in subcutaneous tissues.

b. **Lymphatics or Lymph-vessels.**

(*a*) Lymph Radicles and Lymph Capillaries.—A lymph radicle or rootlet is simply a connective tissue space which is lined with endotheloid plates. These spaces are very irregular, sometimes narrow chinks and crevasses, sometimes comparatively wide spaces.

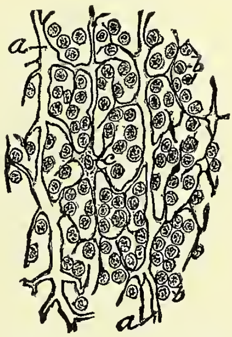
Lymph capillaries conduct the lymph from these irregular *collecting-spaces* to the lymph-vessels. Even the capillaries and the smaller lymphatics are irregular in lumen. (See Fig. 74.)

Fig. 72.



Simple lymph-follicle from conjunctiva of dog: *a*, lymphoid tissue, limited by the fibrous capsule (*b*) *c*, surrounding connective tissue. (After Piersol.)

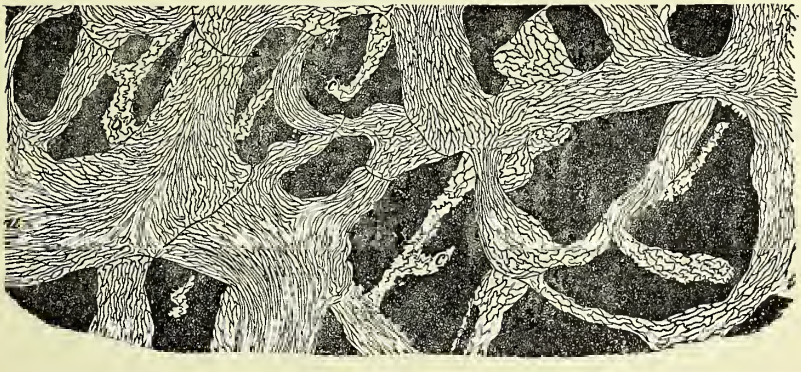
Fig. 73.



Elements of adenoid tissue from partially brushed section of lymphatic gland of child: *a*, fibers of reticulum; *b*, lymphoid cells; *c*, expanded connective-tissue plate. (After Piersol.)

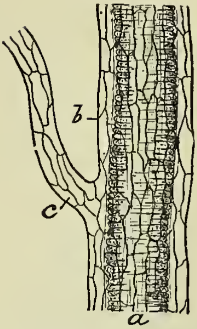
(*b*) Lymph Trunks.—All of the larger lymph-vessels are provided with valves. The larger trunks have a regular lumen and walls quite like those of a blood vessel. (See Figs. 74 and 75.)

Fig. 74.



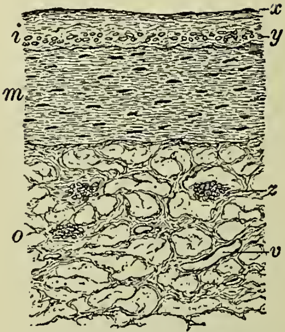
Lymphatic plexus of central tendon of diaphragm of rabbit, pleural side. Klein.) *a*, larger vessels with lanceolate cells and numerous valves; *b*, *c*, lymphatic capillaries with wavy-bordered cells.

Fig. 75.



Perivascular lymphatic (*b*) enclosing a small artery (*a*), from the silvered mesentery of frog; *c*, branching lymphatic capillary. (After Piersol.)

Fig. 76.

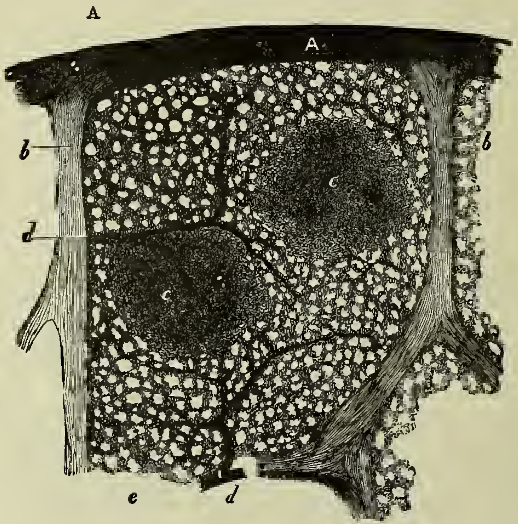


Transverse section of human thoracic duct; *i*, *m*, and *o*, respectively the inner, middle and outer tunics; *x*, endothelial lining, beneath which lies the fibrous stratum containing network of longitudinal elastic fibers (*y*); *z*, longitudinally disposed bundles of muscular tissue within adventitia; *v*, capillary blood vessels. (After Piersol.)

3. THE SPLEEN.

(*a*) Development.—In the human embryo its development begins about the end of the second month. Its beginning may be found in the mesentery posterior to the stomach and immediately dorsal to the duodenum. At this point a very small terminal

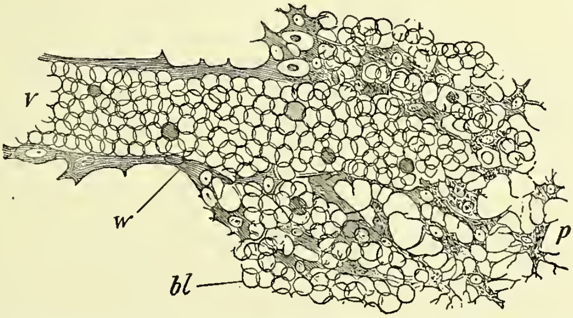
Fig. 77.



Vertical section of a small superficial portion of the human spleen, as seen with a low power. A, peritoneal and fibrous covering; *b*, trabeculæ, *c*, *c*, Malpighian corpuscles, in one of which an artery is seen cut transversely, in the other longitudinally; *d*, injected arterial twigs, *e*, spleen-pulp. (Schaefer after Kölliker.)

branch of the cœliac artery, the future splenic artery, shows in the perivascular lymph channels an accumulation of large lymphoid cells with large granular nuclei. The steps of the development are: The progressive development of lymphatic tissue, the penetration of the mass by terminal branches of the advancing splenic artery, the development of non-striated muscle tissue around the arterial branches and in a coarse mesh-work throughout the mass, the pushing out of the mesentery which forms a splanchnopleuric cover for the spleen, and the definite encapsulement of the organ with connective tissue and non-striated muscular tissue.

Fig. 78.



Thin section of spleen-pulp, highly magnified, showing the mode of origin of a small vein in the interstices of the pulp. *v*, the vein, filled with blood-corpuscles, which are in continuity with others, *bl*, filling up the interstices of the retiform tissue of the pulp; *w*, wall of the vein. The shaded bodies amongst the red blood-corpuscles are white corpuscles.

(*b*) Structure.—Inasmuch as the spleen begins in a development of lymphatic tissue, it is to be expected that its structure is analogous to that of a lymph gland. Such is the case. The spleen sustains to the blood vascular system somewhat the same relation that the lymph glands sustain to the lymph vascular system; and the blood oozes through the spleen reticulum in much the same way that lymph oozes through a lymph gland (Figs. 77 and 78).

4. HISTOGENESIS OF THE CIRCULATORY ORGANS AND TISSUES.

The circulatory system is that system which more than any other is shut off from the outside world. One would expect that this system of organs, which is, *par excellence*, a system devoted to internal relations, should be derived from the entoderm; and it is. You remember that the *entoderm* is early differentiated into hypoblast, mesoblast and notocord. In this differentiation the mesoblast has withdrawn farther from the outside world than was the entoderm. The mesoblast early divides into primitive segments, somatopleure, splanchnopleure and *mesenchyme*. The last named arises latest and is derived from the first three [Hertwig]. From the mesenchyme are derived all the organs and tissues of the circulatory system: (I) The blood itself is purely a derivative of the mesenchyme. (II) The blood vessels and lymphatics are also derived solely from the mesenchyme; viz., the endothelial layer of the intima, the involuntary muscle fibers of the media and the elastic fibers of the vessel walls. (III) The spleen, lymphatic glands and the red-marrow of bones are also wholly mesenchymal tissues,—excepting the splanchnopleuric peritoneum of the spleen. The nerves which supply the muscles of the heart and blood vessels are derived from the ectoderm and are distributed to the circulatory system through the vago-sympathetic nervous system.

C. PHYSICAL INTRODUCTION.

1. THE FLOW OF LIQUIDS THROUGH THE TUBES.

The analogy between the nervous system and a telegraphic system is a striking one and frequently cited; even more striking is the analogy between the circulatory system and the water-supply system of a city. The water-supply starts from a central pumping station,—or elevated reservoir,—passes through large mains at first, and is distributed through branches that are smaller and smaller as they subdivide on their way to different houses. The blood-supply starts from the centrally located, pumping heart, passes through large trunks at first, and is distributed through branches that get smaller and smaller as they subdivide on their way to different tissues.

The physical laws of the circulation are the physical laws of the flow of liquids through tubes. No adequate knowledge of the circulation can be gotten without first a knowledge of the physical laws.

a. The Flow of Liquids under Continuous Pressure.

" *The flow of liquid is caused by a difference of pressure between the different parts of a mass of liquid.*" (Daniell.)

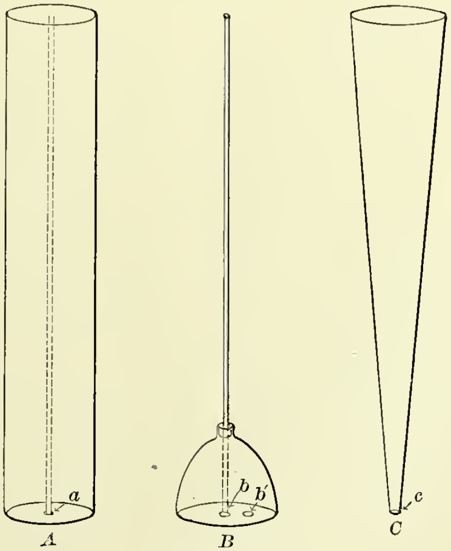
The attraction of the earth—gravitation—furnishes the continuous pressure which causes a flow of liquids along channels or through tubes. The conditions necessary are an elevated source and a low outlet. Let us take, for example, a reservoir as a source of flow. Let an aperture be made in the reservoir any distance (h) below the surface of the water. The pressure upon the water just inside the aperture is greater than pressure at the surface—atmospheric pressure—because it supports the weight of the superposed water. It will therefore flow away from the higher pressure within the aperture toward the lower pressure without the aperture.

1. **Velocity.**—Torricelli's Law: *The rate at which a liquid is discharged through an orifice in the wall of a reservoir is equal to the velocity which would be required by a body falling freely through a height equal to the distance between the orifice and the surface of the liquid.*

From the law of falling bodies we know that *the velocity* (v) *is equal to the square root of twice the product of the height by the acceleration due to gravitation* (g), *i. e.*, $v = \sqrt{2gh} = \sqrt{2 \times 981 \times h} = 44.3 \sqrt{h}$. Velocity thus obtained is expressed in *centimeters per second.*

2. **Discharge.**—Within reasonable limits velocity is not modified by the size of the aperture. Discharge (D) on the other hand, is equal to the product of the area (a) of the jet by the velocity. One would think that the area of the jet would equal the area of the aperture, but such is not the case. The fluid streams toward the aperture from various directions and the jet is, in a way, a resultant of the various streams just referred to and *emerges convergent* to reach a minimum diameter in the "*vena contracta*" very near the aperture. The real diameter of the jet is the diameter of the *vena contracta.* A practical verification of the principle is much simplified by inserting into the aperture a short smooth nozzle. The diameter of the jet will equal the diameter of the nozzle. The discharge (D) equals the product of the area of the jet (a) by the velocity (v), *i. e.*, $D = a \times v$, but $a = \pi r^2$ and $v = 44.3\sqrt{h}$; therefore, $D = 44.3\pi r^2\sqrt{h}$.

FIG. 79.

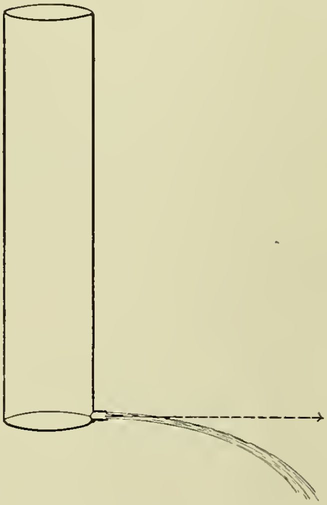


Reservoirs.

Note that 44.3π represents a constant factor that is the same in all experiments; so that the discharge will vary as the square of the radius of the jet and the square root of the height, *i. e.*, D varies as $r^2\sqrt{h}$.

3. **Pressure.**—The pressure may be looked upon as the stress upon the liquid at the point of observation. Take, for example, the pressure of the water on the bottom of a reservoir (Fig. 79). Every square centimeter of the bottom supports the weight of the column of water whose vertical dimension is the depth of the water and whose area (a) is 1 sq. cm. The area of the bottom of the reservoir is not a factor in the pressure. The height of the reservoir, or rather the depth of the water, is the only matter of importance. In reservoir B the pressure upon area (1 sq. cm.) b is the same as that upon area a of reservoir A, because the height of the column is the same. In reservoir C the pressure upon area (1 sq. cm.) c is the same as that upon area a or b, because the area is the same and the height of the column of water is the same. If in reservoir B the pressure on area b is equal to that on area a, so must the pressure on area b' equal that on area a or area b, because *the fluid will transmit pressures equally in all directions.* Then the lateral pressure around the bottom of the reservoir must be as great as the downward pressure. Such is the case. In the reservoir shown in Fig. 80 the pressure at the nozzle would be found by finding the weight of a volume of liquid whose area equals the area of the lumen of the nozzle and whose height is the depth of the liquid above the middle of the lumen of the nozzle.

FIG. 80.

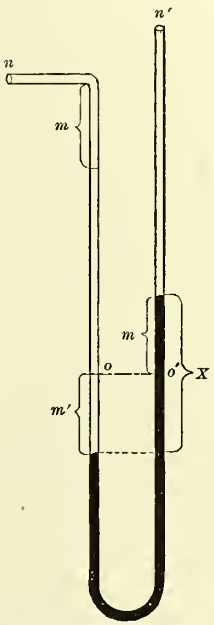


Reservoir with lateral nozzle.

(a) THE MEASUREMENT OF PRESSURE. (a) *The Unit.*—The pressure of the liquid or the stress of the liquid at the point of observation is a form of energy. To express this energy in dynes: P (in dynes per sq. cm.) $= hgs$. $h =$ depth of liquid, $g =$ acceleration of gravitation (981), $s =$ specific gravity. It is customary, however, to express the pressure in height above orifice or "head," and to ignore the factors g and s. This is especially convenient because the pressure is usually measured with a mercury manometer and expressed in "centimeters of mercury," meaning that the pressure is sufficient to support a column of mercury so many centimeters high.

(β) *The Mercury Manometer.*—(See Fig. 81). This instrument consists of a U-shaped tube, one of whose limbs is usually bent at right angles to facilitate its juncture with other apparatus. Both ends of the tube (n and n') are left open. That limb through which the pressure is transmitted (n) is called the *proximal limb*, the other the *distal limb*. When the pressure is positive the mercury will rise in the distal limb; when negative it will fall in the distal limb. The rise in the distal limb (m) will be accompanied by a corresponding fall in the proximal limb (m'); the total pressure will be represented by a column of mercury equal to $2m$ or x. But a part of that pressure is due to an introduced error when the fluid in the proximal tube above the mercury is water or blood, or a salt solution. We have introduced more of this (in centimeters) than was in the proximal tube before.

Fig. 81.



Mercury manometer.

If the fluid which has been introduced with the fall of the mercury in the proximal column is, say, $\frac{1}{13}$ the weight of mercury, then if $m = 13$ cm., the real rise of mercury due to initial pressure is represented by 26 cm. of mercury minus 1 cm. of mercury correction, or 25 cm. mercury. Let us express the relations in more definite terms. Suppose the proximal limb to be filled with water (Sp. Gr. Hg$=$13.596). The corrected height (h) of the column of mercury, when m is the rise in the distal column:

$$h = 2m - \frac{m}{13.596} = \frac{27.192m - m}{13.596} = \frac{26.192m}{13.596}.$$

The pressure in grammes per unit area (p) is equal to the height of the column multiplied by the *Sp. gr.* of mercury.

$$p = hs = \frac{26.192m}{13.596} \times 13.596 = 26.192m.$$

One may readily get the pressure per sq. centimeter by *measuring in cm. the rise of mercury in the distal column and multiplying that by 26.192* (26.2).

The pressure in dynes per unit area (P) is found by simply multiplying p by g, for $P = hgs$ and $p = hs$.

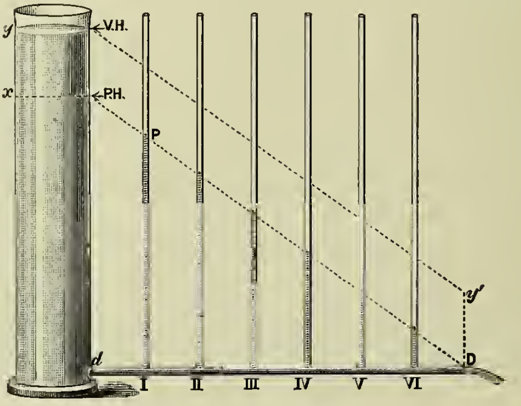
$$P = hgs = 981 \times 26.192m = 25694m \text{ dynes per sq. cm.}$$

To express the pressure in dynes per sq. cm. one has only to observe m and multiply that by 25694.

(γ) *The Piezometer* is a simple instrument consisting of an upright tube connected directly with the point at which the pressure is to be measured. (See Fig. 82, I, II, etc.) The pressure at the bottom causes the liquid to rise in the piezometer until the weight of the column balances the pressure at the base. To compute the P in dynes or the p in gms. one applies the principles given above for the mercury manometer: h equals the rise in the tube as there is no correction in this case. s for water would equal 1; so that $p = h$ and $P = 981h$.

(δ) *Fick's Spring Manometer, the Sphygmoscope, Tambours,* Roy's Piston, and other instruments of the same class are for the observation of varying pressures and are constructed rather for qualitative than for quantitative observations.

Fig. 82.



Reservoir with Piezometers.

(b) The Pressure of Liquid Flowing through Tubes.—Fig. 82 illustrates an experiment with a reservoir, a horizontal delivery tube and a series of piezometers. The piezometers indicate faithfully the pressure of the liquid at the point where they are severally in communication with the delivery tube. The pressure in piezometer I is higher than that in II, that in II is higher than that in III and so on. Note that the pressures are progressively and regularly less as we proceed from the reservoir to the end of the delivery tube. If there were only one piezometer and that located at position VI the water would maintain the same level which it shows in the first experiment. If there were sixty piezometers instead of six, along the same delivery tube the water in every piezometer would rise to the line PD. This line is called the *pressure-slope.*

Why is the pressure less in VI than in V? When the stream of water has reached the point VI it has still to overcome the resistance between that point and the delivery (D). The pressure upward at VI is just the same as the pressure to the right; *i. e.*, the weight of the column of liquid in piezometer VI just balances the "back-pressure" or resistance to the flow to D. Piezometer V measures the resistance beyond V, and therefore must stand higher. The reservoir may be looked upon as a gigantic piezometer. Continue the line DP to the reservoir; the point PH is the *pressure-slope*. All of that head of liquid between the line PHx and the exit (d) of the delivery tube is called the *pressure head* or *resistance head*. The head or stand of liquid below the line PHx represents the quantity of potential energy which is made kinetic and consumed in overcoming the resistance offered by the delivery tube.

What becomes of the potential energy represented by that portion of the water between PHx and VHy? That energy is the source of the velocity with which the liquid jets from the end of the delivery tube. If one wishes to find the velocity he has only to use the distance yx or the distance y'D for h in the formula $v = \sqrt{2gh}$. The stand or head of liquid between PHx and VHy is called the *velocity head*.

The velocity head (VH) plus the pressure head (PH) is called the *driving head* (PH + VH = DH).

In studying the laws of the flow of liquid through tubes under constant pressure we have to consider the following factors: (α) Driving head, (β) resistance head, (γ) velocity head, (δ) lateral pressure as indicated by the piezometers, (ε) resistance.

The solution of the following problems will thrown much light upon the practical problems of the circulation: (I) What is the total effect of increasing or of decreasing the driving head (α)? (II) What is the effect of increasing or of decreasing the resistance (ε), the driving head remaining the same? (III) What is the effect of a simultaneous increase of (α) and increase of (ε)? (IV) The effect of a simultaneous increase of (α) and decrease of (ε)? (V) Decrease of (α) and increase of (ε)? (VI) Decrease of (α) and decrease of (ε)? (VII) How may (γ) be increased without increasing (α)? (VIII) How may (β) be increased without increasing (α)? (IX) What factors cause a variation of velocity? (X) Of lateral pressure?

b. The Flow of Liquids Under Intermittent Pressure.

It is understood by intermittent pressure that the pressure shall be exerted in a rhythmical series of impulses such as is observed in the working of a *pump*.

1. **Intermittent Pressure Through Inelastic Tubes.**—If a pump replace the reservoir of Fig. 82, it will be found that the liquid will flow from the distal end of the delivery tube *in a series of jets* corresponding to the action of the pump, and that the lateral pressure, as indicated by the piezometers, will also vary with the action of the pump, being highest at the moment that the liquid is being driven from the delivery tube with greatest force.

(*a*) With Low Terminal Resistance in the delivery tube the rise and fall of pressure is moderately accentuated.

(*b*) With High Terminal Resistance, such as is afforded by a capillary tube at D, the rise and fall of the pressure within the delivery tube is greatly accentuated.

2. **Intermittent Pressure Through Elastic Tubes.**—Instead of an inelastic delivery tube use a thin rubber tube.

(*a*) With Low Terminal Resistance one notes no essential difference from previous observations with the inelastic tube.

(*b*) With High Terminal Resistance, however, there is a marked transformation in the character of the stream. It issues from the fine terminal capillary *not in jets, but as a continuous and, under favorable circumstances, constant stream.*

How is this accomplished? The sudden influx of liquid thrown into the tube by the pump expands the tube, bringing into play its *elasticity*. When the pump reverses and the valve closes the walls of the tube contract upon the contents and force liquid out of the nozzle while the pump is filling. If the pump acts quickly enough, the jet from the nozzle of the delivery tube may be not only continuous, but quite constant.

The quantity of liquid delivered from a capillary nozzle under such conditions is naturally much greater than the quantity delivered from the same capillary nozzle with an *inelastic* delivery tube. Other advantages will be discussed later.

c. The Flow of Liquids Influenced by Other Factors.

(*a*) The Size of the Tube.—If there were no friction the size of the tube would be of no consequence. The liquid which lies next to the wall of the tube, *i. e.*, the liquid which wets the wall, does not flow at all; the layer next to the wetting layer flows more slowly than any other layer and the layer that is farthest from the wall of the tube flows most rapidly.

The middle, rapidly flowing current has friction against the next external less-rapidly flowing current; and thus a large portion of the kinetic energy may be expended in overcoming friction or resistance. Naturally the larger the tube the smaller the proportion of friction. We may formulate the following law: *The resistance is in inverse proportion to the diameter of the tube.*

Further: *The resistance in a given tube increases with the velocity of flow.*

(*b*) The Change of Course, through bending of the tube causes a change in the distribution of the resistance; (greater in front of the bend and less beyond it) but does not affect the final discharge or velocity.

(*c*) The Effect of Varying Lumen is to cause a variation of the velocity with the varying lumen. "Leonardo da Vinci," who was a great hydraulic engineer as well as a great painter, formulated this law: *The velocity of the current at any point is inversely proportional to its cross-sectional area.*

The cross-sectional area of the capillaries taken together equals 500 to 700 times the cross-sectional area of the aorta.

(*d*) The Effect of Branching is to introduce eddies and whirls into the stream. This causes increased resistance. If the ramification of the tubes leads to greater sectional area the velocity will decrease proportionally; if to smaller sectional area the velocity will increase proportionally.

D. HISTORICAL INTRODUCTION.[1]

1. ARISTOTLE.

Dalton thus summarized the ideas entertained by Aristotle, regarding the heart and blood vessels:

"I. The heart is an organ for giving to the blood its final elaboration, and for communicating to it the necessary element of vital heat.

"II. The perfected blood is received from the heart into the blood vessels arteries and veins alike, and brought by their branches and ramifications into proximity with the solid tissues which it nourished by exudation.

"III. The pulsation of the heart is a momentary dilatation from expansion of the blood in its cavities; this expansion being produced by the animal heat combining with the ingredients of the blood. The pulsation of the blood vessels is due to the same cause, and is simultaneous with that of the heart; the impulse originating in the cardiac cavities being at once communicated to the blood in every part."

It may be added that Aristotle followed Hippocrates in the use of the word artery (ἀρτηρία) for the *trachia* and not for a blood vessel.

2. PRAXAGORAS.

The predecessors of Praxagoras believed that all of the blood vessels pulsate. Praxagoras showed that the vessels could be divided into two classes, the blood vessels (veins) and the air vessels (arteries), to which he appled the old term *ἀρτηρία*, distinguishing these air vessels from the trachia by calling the latter the "rough air-tube," *ἀρτηρία τραχεῖα.*

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[1] For the facts briefly summarized here the author is indebted to Dalton's admirable little volume on the *Doctrines of the Circulation.*

3. THE ALEXANDRIAN SCHOOL.

This school was founded by Ptolemy. It was a real university. Here Euclid taught geometry; Archimedes taught physics; Strabo and Eratosthenes taught geography, and Hipparchus and Ptolemæus taught astronomy.

Among the great teachers of medicine were Herophilus and Erasistratus. "It was in their time and at the Alexandrian school that the dissection of the human body was first legalized," * * * by the Ptolemies, the bodies of condemned criminals being devoted to this purpose. Notwithstanding these facilities, it was anatomy and not physiology which was the gainer. It was at this school that the *pneuma theory* (see General Introduction) was first elaborated. The teachings of Praxagoras and Aristotle, as outlined above, were accepted and taught for four or five centuries.

Erasistratus accurately described the valves of the heart, but he did not know their function. "The diastole of the heart, in the physiology of the period, is an *active* expansion, drawing into the right ventricle, as if by suction, a little *blood* to be used for the nourishment of the lung, and into the left ventricle a little *pneuma* (air) to supply the arteries."

"The terminal ramifications (of the blood vessels) are so small that the blood is retained within them by the 'coaptation' of their walls. Consequently, although the mouths of the vein and the artery lie side by side, the blood, nevertheless, remains in its own vessels, and *nowhere penetrates into those of the pneuma, when the system is in its normal condition. But when, from any disturbing cause, the blood is forced over from the veins into the arteries a morbid action results.*"

4. GALEN.

By dissections Galen determined the structural features of the fœtal circulation and the changes which take place in the circulatory system after birth. As Galen resorted to vivisection, he was able to refute some of the ancient dogmas which were based upon the observation of the dead body, and some of the hypotheses regarding the living body.

The first notable advance made by Galen was his demonstration that the *arteries normally contain blood.* His part of the controversy regarding this subject appears in a special treatise entitled: "*Whether the arteries naturally contain blood.*" (Galenius, Opera Omnia, Vol. IV., p. 703.)

"The general features of Galen's physiology are to be found in his books on: *The Functions of the Parts; The Causes of the Pulse; The Use of Respiration; The Physiological Forces.*

"In this system the liver was the central organ of nutrition and sanguinification. From it all the veins took their origin, and in its glandular tissue the blood was prepared from the elements of the digested food, brought to it by the portal vein." * * * "The blood in the venous system provided for the general nourishment of the tissues. On the other hand, the arteries were also full of blood, but of a different kind. The venous blood was dark, thick and rich in the grosser elements of nutritive material. The arterial blood was thinner, warmer, bright-colored, and, above all, *spirituous; i. e.*, it contained an abundant supply of the vital spirits, which it distributed throughout the body. Its warmth it obtained from the heart, and especially from the left ventricle in which the animal heat was generated; its vital spirits being * * * derived from the inspired air of the lungs. *Thus the arteries contained vital spirits, not in the form* of a distinct gaseous body, but amalgamated with the other ingredients of the blood." "As the liver was the origin of the veins, so the heart was the origin of the arteries."

The phenomenon of the *pulse* was thus explained: "This is a force of *active expansion* dilating the artery and attracting the fluids into its cavity *from either direction;* while its subsequent contraction causes an expulsion of its contents *toward every point.*" * * * "The heart dilates to attract the necessary materials; remains fixed while using what it has drawn into it; and contracts when discharging its superfluities." * * * "The various acts of reception and delivery are thus accomplished by the cardiac movements *aided by the valves.*"

"The functions of the heart and blood vessels are inseparably connected with the act of respiration." * * * "The prime object of respiration is the introduction of the *pneuma*, or *spirits*, the characteristic ingredient of arterial blood."

Recall that Erasistratus and the Alexandrian school had taught that the blood might pass from veins to arteries, under abnormal conditions, wound or inflammation. Galen says, "*The arteries anastomose with the veins over the whole body, and they mutually receive from* each other *blood and spirits* (πνεῦμα) *through certain invisible and extremely minute passages.*" (Passages, in the tissue, and in the intraventricular septum.) (Galenius, Opera Omnia, Vol. III., p. 455.)

Note that the communication of the veins and arteries was not an observed fact in Galen's time, but *an hypothesis to account for observed facts.*

For the influence of Galen's doctrine upon medical teaching see General Introduction.

5. VESALIUS.

Galen's knowledge of anatomy and physiology was gained largely from his surgical operations and from dissection and vivisections of lower animals. Vesalius founded his anatomy upon the human body. This led to many points of controversy between Vesalius and Galen and naturally hindered the acceptance of the views of Vesalius by his contemporaries who were disciples of Galen. Vesalius was professor of anatomy at three universities in Italy (Padua, Bologná, Pisa), visiting each in turn. At that time anatomy and physiology had not been recognized as separate departments of biological science. Vesalius, though radical in his anatomy, was conservative in his physiology, accepting the former doctrines with slight modifications. He did not accept without question Galen's theory that the venous and arterial blood communicated through the intra-ventricular septum.

Regarding the communication between different sets of vessels in the tissues Vesalius says: "The branches of this vein (the vena cava) distributed through the body of the liver, come in contact with those of the portal vein; and the extreme ramifications of these veins *inosculate with each other, and in many places appear to unite and* be continuous. (Vesalius, *De Humani corporis fabrica.* Lib. VI., Cap. XV.)

6. SERVETUS.

This unique character was a theologian, lawyer, and physician by education though he never successfully practised any of these professions. In both theology and medicine he was a heretic and because of the enthusiasm of his heresy he scarcely escaped being classed as a criminal in the eyes of the law. The great work of his life was a book entitled: "*Christianismi Restitutio.*" In this book, which was a plea for the restoration of Christianity to its original form, he had occasion to discuss at length the "'Divine Philosophy' of the life and spirits in the corporeal frame. After giving the usual account of the vital spirits as produced in the heart, and the animal spirits in the brain, he proceeds to explain how it is that the life, or soul, is not seated in the substance of the solid organs, but in the blood, and that the life itself is the blood as taught by Holy Writ." * * * "It [the vital spirit] is generated from the mixture made in the lungs between the inspired air and the finely elaborated blood which the right ventricle of the heart communicates to the left. *This communication, however, does not take place through the median wall of the heart, as commonly believed; but, by a grand device, the refined blood is driven from the right ventricle of the heart, in a long course through the lungs. By the lungs it is prepared, assuming a bright color, and from the vena* *arteriosa* [*pulmonary artery*] *is transferred into the arteria venosa* [*pulmonary veins*]." * * *

"By means of the same device, which in the liver makes a transfusion from the portal vein to the vena cava for the blood, there is in the lung a transfusion from the vena arteriosa to the arteria venosa for the spirit." (Servetus—Translated by Dalton.)

"His account of the mode of communication, in the lungs, between the two sets of vessels is very striking; he says that it is by, 'another kind of vessel, formed from the vein and the artery,' as if he had devined the existence of the pulmonary capillaries" (Dalton).

7. COLOMBO.

Colombo, a pupil of Vesalius, demonstrated, "that that portion of the blood which was to replenish the arterial system passed from the right side [of the heart] to the left through the lungs, and, furthermore that *its arterialization took place in these organs, and not in the ventricle.*"

He demonstrated by vivisection that the pulmonary veins do not pulsate. He did not know of the branchial arteries and supposed that a portion of the blood which passed to the lungs from the right side of the heart went for the nourishment of the lung substance.

8. FABRICUS.

Hieronymus Fabricus demonstrated the existence of the *valves* as "a general feature of the venous system, and described them in such a way that there was no longer any uncertainty as to their reality or importance."

All the dissections, and vivisections and speculations of the anatomists and physiologists had not, up to the end of the seventeenth century, revealed the fact that there must be return to the circulatory centers—liver and heart as then understood—from the periphery, but the veins as well as the arteries were supposed to carry efferent streams into peripheral parts—legs, arms, head. The prodigious inconsistencies attending this theory neither seemed to arouse question, nor to incite to investigation.

9. HARVEY.

In 1628 William Harvey published a work on the circulation (Harvey, *De Motu Cordis et Sanguinis.* Frankfort, 1628).

In this remarkably concise and conclusive treatise Harvey summarizes the work of nine years of investigation on the circulation. He successfully demonstrates:

(I) That the heart passively dilates and actively contracts; (II) that the auricles contract before the ventricles do; (III) that the contraction of the auricles forces the blood into the ventricles; (IV) that arteries "have no 'pulsific' power," *i. e.*, they dilate passively, "since the pulsation of the arteries is nothing else than the impulse of the blood within them;" (V) that the heart is the organ of propulsion for the blood; (VI) that in passing from the right ventricle to the left auricle, "the blood transudes, through the pulmonary parenchyma, from the right ventricle of the heart into the arteria venosa (pulmonary veins) and the left ventricle; (VII) that the quantity and rate of passage of blood peripherally from the heart makes it a physical necessity that most of the blood return to the heart; (VIII) that the blood does return to the heart by way of the veins; Harvey could not find evidence of anastomosis between arteries and veins and did not believe that such existed. He believed that the blood *filtered through the tissues.*

He demonstrated to the full satisfaction of most of his colleagues that the blood made a complete circuit of the arteries and veins propelled by the heart, *i. e.*, he demonstrated the *circulation* of the blood.

10. MALPIGHII.

Marcello Malpighii, made professor of medicine in Bologna University in 1661, had the aid of a microscope and was therefore in a position to clear up the problem as to how the blood passes from the arteries to the veins. *Malpighii demonstrated the capillary circulation in the lung of a frog.*

THE PHYSIOLOGY OF CIRCULATION.

A. CLASSIFICATION OF THE FLUIDS, TISSUES AND ORGANS.

B. THE CIRCULATING FLUIDS.

1. THE BLOOD.
    - I. THE PHYSICAL PROPERTIES.
    - II. THE MORPHOLOGY OF THE BLOOD.
        - *a.* The Red Blood Pressure.
        - *b.* The White Blood Corpuscles.
        - *c.* Other Morphotic Elements.
    - III. THE CHEMICAL PROPERTIES OF THE BLOOD.
    - IV. THE FUNCTIONS OF VARIOUS PORTIONS OF THE BLOOD.
    - V. THE TOTAL QUANTITY OF BLOOD IN AN ANIMAL.
    - VI. THE PROTECTION OF THE BLOOD SUPPLY.
        - *a.* The Location of the Vessels.
        - *b.* The Coagulation of the Blood.
    - VII. THE EFFECT OF HEMORRHAGE.
    - VIII. THE TRANSFUSION OF BLOOD.
    - IX. THE PHYSIOLOGICAL VARIATIONS OF THE BLOOD.
2. THE LYMPH.
    - I. THE PHYSICAL PROPERTIES.
    - II. THE MORPHOLOGY OF THE LYMPH.
    - III. THE CHEMICAL PROPERTIES OF THE LYMPH.

C. THE FORMATION AND DESTRUCTION OF THE CORPUSCLES.

1. THE FORMATION OF RED BLOOD CORPUSCLES.
2. THE DECAY AND DESTRUCTION OF THE RED BLOOD CORPUSCLES.
3. THE FORMATION AND DESTRUCTION OF LEUCOCYTES.
4. SUMMARY OF THE FUNCTIONS OF THE SPLEEN.

D. THE CIRCULATION OF THE FLUIDS.

1. THE ACTION OF THE HEART.
2. THE CIRCULATION OF THE BLOOD.
    - *a.* The Circulation in the Arteries.
    - *b.* The Circulation in the Capillaries.
    - *c.* The Circulation in the Veins.
3. THE CIRCULATION OF THE LYMPH.
    - *a.* In the Lymph Radicles.
    - *b.* In the Lymphatics.

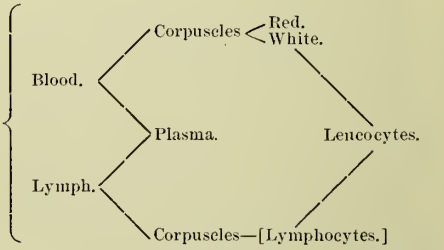
E. THE CONTROL OF THE ORGANS OF CIRCULATION.

1. THE INNERVATION OF THE CIRCULATORY SYSTEM.
    - *a.* The Innervation of the Heart.
    - *b.* The Innervation of the Arteries.
2. ADAPTATIVE COÖRDINATIVE OF THE ACTIVITIES OF THE CIRCULATORY ORGANS.

THE PHYSIOLOGY OF CIRCULATION.

A. CLASSIFICATION OF THE FLUIDS, TISSUES AND ORGANS.

Fluids of the Circulatory System.



Tissues and Organs for the Formation or Destruction of Corpuscles.
- Red Marrow of Bones.
- Lymph Glands.
- Spleen.

Organs of Transmission of Fluids.
- Of Blood.
  - Heart.
  - Arteries.
  - Capillaries.
  - Veins.
- Of Lymph.
  - Lymph-radicles.
  - Lymphatics.

Organs of Control.
- Cranial Centers
  - Cardiac.
  - Vaso-motor.
- Parts of Vago-Sympathetic System.
- Vaso-Motor Nerves.

B. THE CIRCULATING FLUIDS.

1. THE BLOOD.

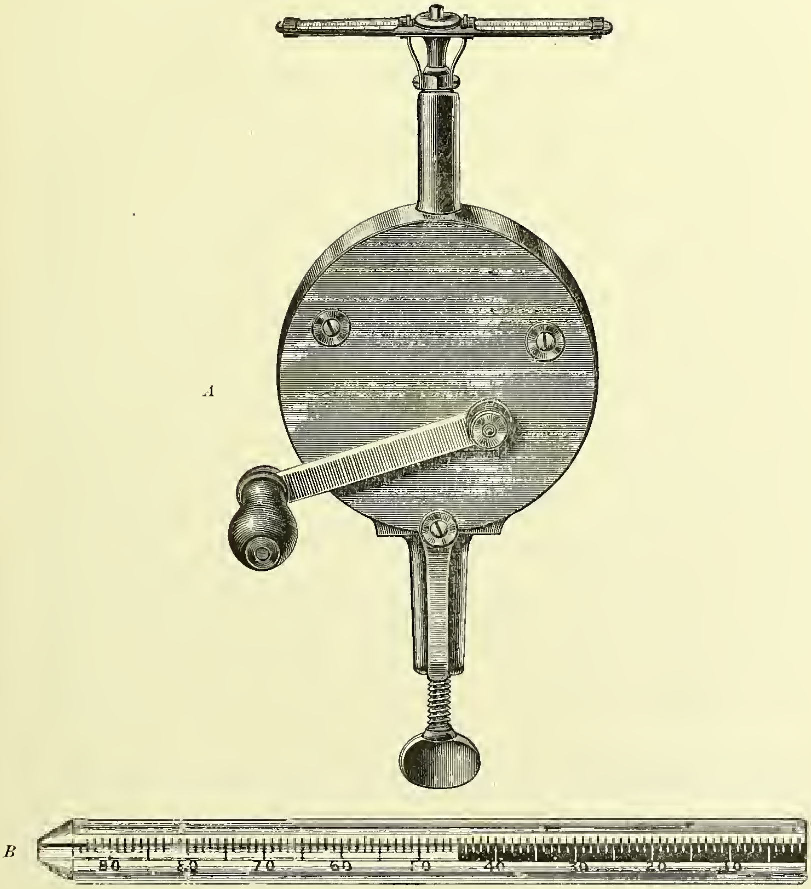
I. THE PHYSICAL PROPERTIES.

1. **Physical Constitution of the Blood.**—*The blood is a liquid.* The fact that the blood is not transparent leads at once to the conclusion that it is not a homogeneous liquid, but that there are particles held in suspension. Johannes Müller succeeded in separating the liquid from the suspended particles by filtration. Before that time, however, the microscope had revealed the fact that the particles were corpuscles or cells,—highly specialized cells, however. The liquid in which the *corpuscles* are suspended is called liquor sanguinis or *plasma.* There are three methods of procedure in separating blood into its physical components:

(*a*) By Filtration.—Johannes Müller succeeded in filtering frog's blood after adding to it a small quantity of $MgSO_4$ or

Na_2SO_4 or $\frac{1}{2}$ per cent. sugar. He failed to filter mammalian blood after the same method; but Alex. Schmidt has done so repeatedly with horse's blood if proper precautions are taken, instantly subjecting the drawn blood to 0°C., mixing with 20 per cent. of its volume of Na_2SO_4; and filtering after an hour or two.

FIG. 83.



The hæmatocrit. The attachment at the upper end of the vertical shaft is made to rotate at a speed of 7000 to 10000 per minute by means of the gear-work of the body of the instrument. Each arm of the rotating attachment is provided with a capillary tube which is graduated into 100 divisions. If the tube be filled with blood and rotated for 2 or 3 minutes at the speed above mentioned the corpuscles will be thrown to the outer end and the volume per cent. may be read off on the tube. An enlarged view of tube with centrifugalized blood.

(*b*) BY SUBSIDENCE.—If the blood of a mammal,—especially of a horse,—be mixed as above described, with 20 per cent. of its volume of saturated solution of $MgSO_4$ or Na_2SO_4 and subjected instantly to freezing temperature it is found that the corpuscles will sink to the bottom leaving the clear plasma above. This is facilitated by oiling the inner surface of the receptacle. If the conditions are very favorable the blood from the jugular *vein* of a horse may separate without the addition of the salt solution.

(*c*) By Centrifugation.—If the blood of any animal be drawn into a capillary tube and instantly subjected to centrifugation the heavier corpuscles are thrown to the outer end of the tube and the separated plasma and corpuscles may be quantitatively determined. Fig. 83 shows a centrifuge or hæmatocrit; a speed of 7,000 to 10,000 rotations per minute is sufficient to throw all the corpuscles to the outer end of the tubes in 2 or 3 minutes. The volume per cent. may be read off on the graduated capillary tube.

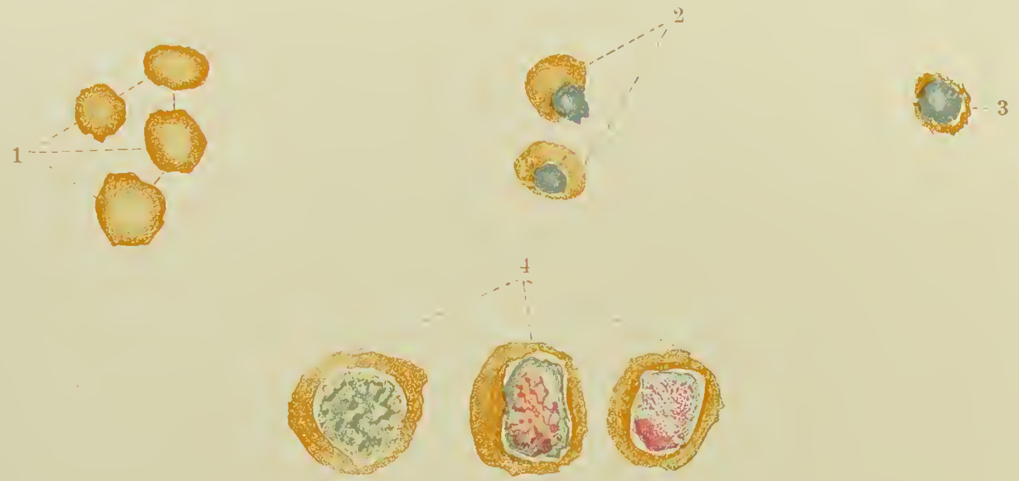
2. **Color.**—The color of the blood in the body varies from light scarlet in the arteries to a dark bluish-red in the veins. Owing to the physical properties mentioned above the blood is opaque—even thin layers of it obstructing the light. The bright red color of the albino's eyes is due to the blood of the central artery of the retina—unobstructed from view by the translucent iris. The pink color of the lips, nails, conjunctiva and oral mucous membrane in health is due to the blood. If the blood is lessened in quantity as in anæmia the pink gives place to a pale or even waxy white color ; while in asphyxia and certain serious heart lesions these parts take on a ghastly bluish color.

3. **Odor.**—Any one who has been present at a slaughtering has noticed the peculiar odor emitted by the freshly shed blood. This odor is somewhat different in the blood of different animals and is due to the presence in somewhat varying relative amounts of volatile fatty acids. In blood which has been shed for some time the odor may be revived by liberating these volatile fatty acids with concentrated H_2SO_4.

4. **Taste.**—Blood has a saline taste due to the salts dissolved in the plasma.

5. **Specific Gravity.**—The specific gravity of the blood as a whole is 1056 to 1059 in man, and 1051 to 1055 in woman ; in children it is less and is subject to greater variations. This is a composite specific gravity made up of plasma 1007 and blood corpuscles 1105. It is due to this difference in the specific gravity of the plasma and corpuscles that separation by sedimentation or by centrifugation is possible. As the specific gravity of the blood has some clinical importance it may be determined as follows (Landois): Take 10 small beakers each containing a few c.c. of Na_2SO_4, the first beaker containing a solution having Sp. Gr. of 1050, the next 1052, and so on. Eject a small drop of blood into each in turn, from the horizontally placed tip of a pipette and watch the results: if it sinks in 1050, remains stationary in 1052 and rises in 1054, the Sp. Gr. is 1052.

PLATE I.



Varieties of Red Corpuscles.

1. Normal Red Cells.
2. Normoblasts.
3. Microblasts
4. Megaloblasts.

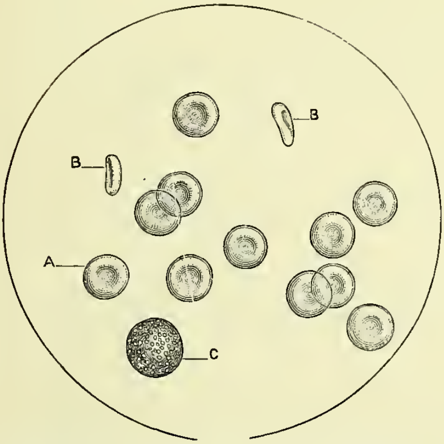
2. THE MORPHOLOGY OF THE BLOOD.

a. The Red Blood Corpuscles.

1. **Form.**—The red blood corpuscles of man are *circular, biconcave discs.*

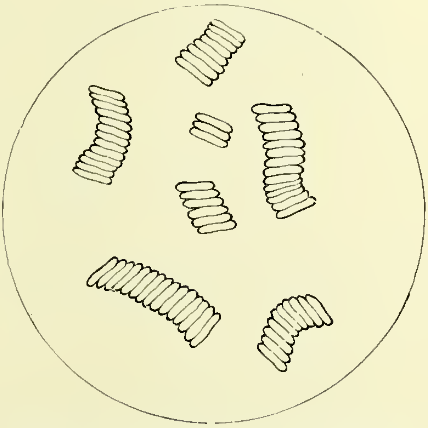
The accompanying figure (Fig. 84) shows the typical corpuscles when seen under the most favorable circumstances, floating in fresh plasma.

Fig. 84.



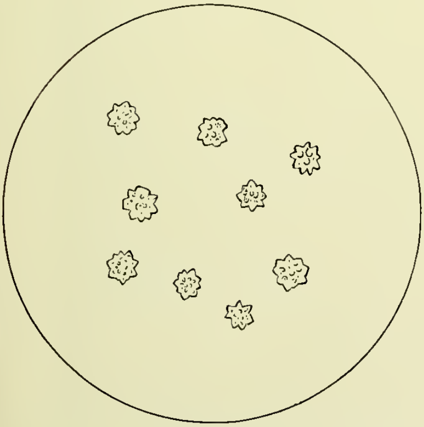
Human blood corpuscles. *a*, red corpuscles, seen flatwise; *b*, red corpuscles, seen edgewise; *c*, white corpuscles. (Dalton.)

Fig. 85.



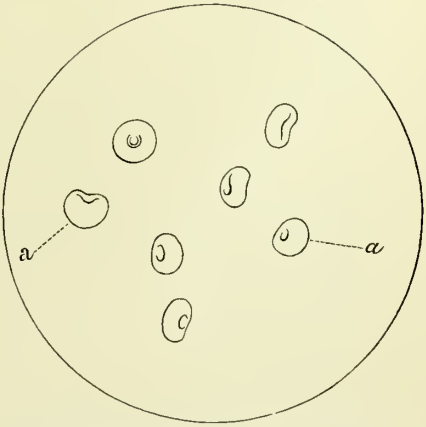
Red globules of the blood, adhering together, like rolls of coin. (Dalton.)

Fig. 86.



Red corpuscles of the blood, shrunken, with their margins notched. (Dalton.)

Fig. 87.



Red corpuscles of blood, after the imbibition of water. (Dalton.)

If the film of blood is somewhat deep and the glass on which it is spread is jarred or shaken the discs readily form into roulettes like rolls of coins (see Fig. 85). If after being drawn the blood is exposed to the air too long, or if the plasma be diluted with a hyperistónic fluid, or fluid of greater density than the plasma the red corpuscles become crenated as shown in Fig. 86. If on the other hand the plasma be diluted with a hypisotonic fluid, *i. e.*, of less density than the plasma, the corpuscles at once swell and assume a form shown in Fig. 87, finally becoming quite spherical. If pure water be used the hæmoglobin will be gradually dissolved and the corpuscles appear bleached out. Let a very thin film of blood be "spread" upon a cover glass, "fixed" by heating at 100° C., and stained with a fluid of the following formula :

Ehrlich-Bondi powder (Grübler).............	1 gm.
One-half per cent. acid Fuchsin............	5 c.c.
Aqua dist..............................	25 c.c.

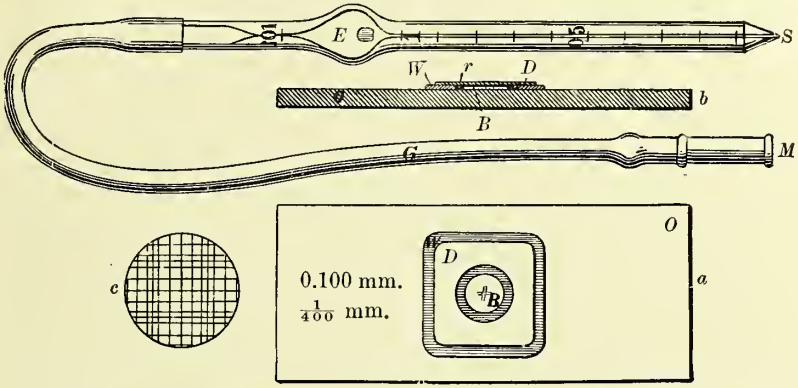
Most of the red corpuscles of the field will have the form shown in Plate I. (1). An occasional one may have one of the other forms : Normoblasts, (2), microblasts, (3), or megaloblasts, (4).

2. **Size.**—There are two methods of determining the size of a microscopic object. (I) Its image may be projected upon a scale by a camera lucida and the dimensions determined. (II) A much more convenient method is to measure directly, objects in the field of the microscope, with the aid of an eyepiece micrometer. By one or the other—usually the latter—of these methods the average diameter of the red blood corpuscles has been determined, and is 7.7 μ, or 7.7 micro-millimeters [a micro-millimeter is one-thousandth of a millimeter]. It has been found that there is considerable variation in these dimensions, measurements of normal corpuscles varying from 6.7 μ to 9.3 μ. The maximum thickness of a red blood corpuscle is about 1.9 μ. The size is somewhat diminished by septic fever, asphyxia, or the administration of considerable morphia; and is increased by alcoholism, quinine, or watery condition of the blood. The size of the red blood corpuscles has had considerable medico-legal importance ; but the fact that the corpuscles of animals frequently associated with man fall within the limits of variation of human corpuscles, has led to a general distrust of this evidence. The average diameter of the red blood corpuscles of a dog is 7.3 μ (varying from 6.6 μ to 9 μ), of a cat 6.5 μ and of a rabbit 6.9 μ.

3. **Number.**—(*a*) THE INSTRUMENTS USED TO COUNT THE CORPUSCLES.—The total number of corpuscles can only be estimated. The number pro unit volume can be exactly determined by such instruments as the Gower's Hæmacytometer or the Zeiss

blood-corpuscle counter. The use of either of these instruments involves the dilution of the blood with a known quantity of some other liquid. Fig. 88 shows a Zeiss counter in its case. The instrument consists of a diluting pipette and a ruled slide for the microscope stage. In diluting the blood the observer draws from a fresh drop of blood a quantity sufficient to fill the pipette to the line marked 1, then a quantity of the diluting fluid sufficient to fill the pipette to the line marked 101. The mixing chamber of the pipette contains 100 volumes of fluid, one of which is blood. The inner circle of the slide is ruled into squares whose sides are $\frac{1}{20}$ mm. The ring surrounding the inner circle is a groove whose office is to receive the excess of blood placed upon the inner surface.

Fig. 88.

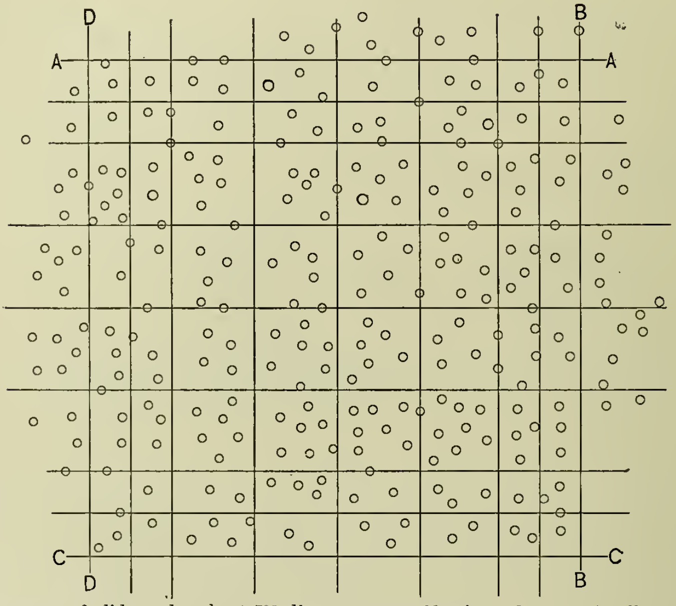


The Thoma-Zeiss blood-counter. The mixing pipette in which each volume of blood is diluted to 100 to 200 volumes. *A*, *B* and *C*, plan and elevation of the counting slide.

The quadrangular plate outside of the groove stands $\frac{1}{10}$ mm. higher than the ruled circle. When a cover-glass rests upon the quadrangular plate it incloses over each square of the ruled circle a volume of fluid whose dimensions are $\frac{1}{20}$ mm. × $\frac{1}{20}$ mm. × $\frac{1}{10}$ mm. = $\frac{1}{4000}$ cubic mm.

(*b*) The Use of the Zeiss Corpuscle Counter.—One dilutes the blood as directed above, mixes it thoroughly by shaking, and forces out a drop of the mixture upon the ruled circle. The cover-glass is put in place, the slide brought under the focus of a microscope and the average number of corpuscles determined in each square. This average is multiplied by 400,000 to get the number of red blood corpuscles in one cubic millimeter of blood. If one uses pure water the corpuscles will swell; if one uses 2 per cent. salt solution they will shrivel. If the number alone is to be determined this change in size is of little importance, and one may dilute with a 2 per cent. solution of sodium chloride. If, however, one wishes to determine number and size at the same time it is necessary to dilute the blood with a fluid which will not extract water from the corpuscles, *i. e.* with an isotonic fluid. Such a fluid is the aqueous humor of the eye, which may be collected in sufficient quantity in sterilized pipettes from fresh ox-eyes, using one pipette for each eye. More usual is blood serum, collected from a clot. The difficulty of having these fluids always at hand makes the use of an "artificial serum" most advisable.

Fig. 89.



Appearance of slide under about 500 diameters magnification. One counts all corpuscles which lie upon the right and lower boundaries of each square.

Artificial serum :

Solution of gum arabic	(sp. gr. 1020)	20 c.c.
" NaCl	(" " ")	30 c.c.
" Na_2SO_4	(" " ")	30 c.c.
		80 c.c.

Using this fluid one may with an eye-piece *micrometer* and a Gower or Zeiss *counter* determine at once the size and the number per unit volume. The normal average number of red blood corpuscles per cubic millimeter of blood is, in man 5,000,000, in woman 4,500,000. In any particular specimen of blood the number of red blood corpuscles per cubic millimeter will vary with varying proportions of plasma and corpuscles. It follows then that anything which tends to increase the volume of the blood plasma will decrease the number of corpuscles per cubic millimeter of blood; while anything which tends to decrease the volume of the plasma will increase the number of corpuscles per cubic millimeter of blood; *i. e.*, the relative number of red blood corpuscles varies inversely as the amount of plasma. The relative number of red blood corpuscles will be increased by the passage of the blood through cutaneous arterioles and capillaries, after use of solid food, and after free perspiration, diuresis or diarrhœa. The relative number of red blood corpuscles will be decreased by the passage of the blood through intestinal capillaries after a fluid meal; also by any causes leading to sudden decrease in perspiration or excretion of water from the kidneys.

If the corpuscles do not vary in size it is clear that in successive examinations of the blood of the same individual the proportions of red corpuscles found by centrifugation will be approximately proportional to the number per cubic millimeter. If the corpuscles vary in size the number will not be proportional, an increase in number being accompanied by a corresponding decrease in size.

(*b*) **The White Blood Corpuscles or Leucocytes.**

These cells are composed of unmodified protoplasm. They are wholly unspecialized and are the potential equivalents of a primitive unicellular animal; *e. g.*, the amœba. They are identical with the lymph corpuscles and with the wandering connective tissue cells. In summing up their physical and morphological characters Landois says: "These cells consist of more or less spherical masses of protoplasm which is sticky, highly refractile, soft, mono- or multi-nucleated, capable of amœboid movement and devoid of an envelope [cell membrane]." They vary much in size—4 μ to 13 μ—as well as in numerical proportion to the red blood corpuscles, the average proportion being 1 to 350. This proportion is increased during pregnancy, after parturition, and is very much decreased by fasting. This proportion may be determined while making a count of the red corpuscles. It is necessary to stain the white corpuscles in order to be able to readily distinguish them from the red. To this end Toisson's solution is used as a diluting fluid.[1]

---

[1] Toisson's solution:

Methyl violet 5 b.	.025
NaCl	1
Na_2SO_4	8
Glycerine	30
Aqua dist. q. s. ad.	200

This is to be used 1–200; *i. e.*, fill the diluting pipette to the line 0.5, instead of 1, with blood before diluting.

The abnormal increase in the relative number of leucocytes is characteristic of the disease leukæmia; and may be associated with other affections of the blood or blood-forming organs.

The minute structure of the leucocyte is not revealed to the eye without the use of some system of differential staining. To Ehrlich we are indebted for the first systematic work in this field. He found that granules in the cytoplasm reacted differently to acid, neutral and basic stains. The granules which take the acid stain, eosin, he called *eosinophiles*, those which take the neutral dyes he called *neutrophiles*, and so on, differentiating different classes of granules. As the subject was studied it was found that classification of the leucocytes, according to their reaction to the stains, is convenient and valuable clinically. The term eosinophile and neutrophile has come to be applied to the leucocyte and not to the granules alone. The most common leucocyte is the polymorpho-nuclear neutrophile, or simply *neutrophile;* also found sparingly in normal blood is the *eosinophile.* The accompanying plate (Plate II.) gives the varieties of leucocytes.

There may be an abnormal proportion of the normal leucocytes or there may be an appearance, in considerable numbers, of the rarer forms of leucocyte. This subject is discussed *in extenso* in the clinical treatises on the blood.

c. Other Morphotic Elements of the Blood.

1. **Blood Platelets of Bizzozero** are "pale, colorless; oval, round or lenticular discs of variable size"—av. 3 μ—whose origin, function and destiny are yet under discussion, and the confusion of theories makes it unsafe to venture an opinion. This much, however, seems certain: The plates disintegrate directly after the shedding of blood, and inasmuch as the microscope reveals little clumps of the granular débris of the plates where the fibrin fibrils cross, the theory that these problematic bodies are active agents in coagulation seems to have a justifiable basis. The part they play is probably to furnish one source of the fibrin ferment.

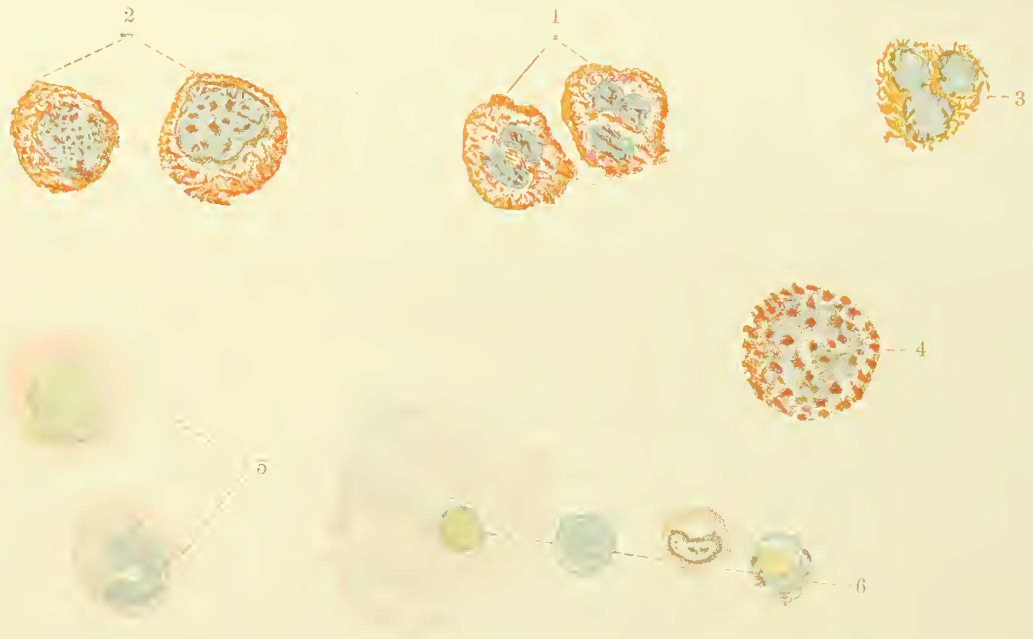
2. **Elementary Granules** are minute particles of proteid matter probably arising from the disintegration of white corpuscles or of the blood-platelets.

III. THE CHEMICAL PROPERTIES OF THE BLOOD.

a. Chemical Composition.

Analysis of the blood proves it to be composed of 775 to 800 parts of water and 200 to 225 parts of solids. The solids are

PLATE II.



Varieties of Leucocytes.

1. Polymorphonuclear Neutrophiles.
2. Myelocytes.
3. Eosinophile.
4. Eosinophilic Myelocyte.
5. Large Lymphocytes.
6. Small Lymphocytes.

192 to 217 parts of organic and 7 to 8 parts of inorganic matter. The organic matter is composed of hæmoglobin, of proteids, fats, and traces of sugar, while the inorganic matter is composed of $NaCl$, KCl, $NaHCO_3$, Na_2HPO_4, $CaHPO_4$, $CaSO_4$, $MgCl_2$, etc.

The best idea of the chemical composition of the blood as a whole may be obtained by first separating the blood into plasma and corpuscles by centrifugation, and then analyzing each separately. Human blood so treated would give approximately the results recorded in the following table, which is the result of an analysis reported by Halliburton :

Chemical composition of Blood.	Plasma Av. 52%. Max. 567. Min. 456. Take 100 parts.	Water						90.29%
		Solids 9.71%	Organic 8.86%	Proteids	Serum Albumin Serum Globulin			7.9 %
					Fibrin			0.4 %
				Extractions : Fats, etc.				0.56%
			Inorganic 0.85%	Soluble Salts.	$NaCl$ KCl $NaHCO_3$ Na_2HPO_4			0.85%
				Insoluble Salts.	$CaHPO_4$ $CaSO_4$			
								100.00
	Corpuscles. Av. 48%. Max. 54.4%. Min. 43.3%. Take 100 parts.	Water						68.80%
		Solids 31.2%	Organic 30.4	Proteids 29.79%.	Hæmoglobin 27	Hæmatin	Fe.	27.36%
						Globulin		
					Globulin			2.43%
				Fats.	Lecithin Cholesterin			0.61%
			Inorganic 0.8%	KCl $NaCl$ $MgCl_2$ $CaHPO_4$ $Mg_3(PO_4)_2$ Fe. [See Hæmatin.]				0.80%
								100.00

Reaction.—The reaction of the blood arises not from any peculiarity of the corpuscles but from the plasma. This fluid is a complex one and among other constituents contains Na_2HPO_4 and $NaHCO_3$ which give it an alkaline reaction in freshly shed blood ; but shed blood rapidly loses its alkalinity.

The average alkalinity of the blood is equal to that of a 0.2 per cent. solution of sodium hydrate. The reaction of the blood may be qualitatively determined by placing a drop upon the surface of a plaster of Paris disc which has been impregnated with neutral litmus. If after a moment's contact the blood be wiped off the faint blue will be seen. The alkalinity of the blood may be decreased during health by (I) great muscular exertion, and (II) by exposure of the blood to the conditions of coagulation. Pathologically the alkalinity of the blood may be *increased* by persistent vomiting, and *decreased* by (I) anæmia, (II) uræmia, (III) rheumatism, (IV) high fever, (V) diabetes, (VI) cholera.

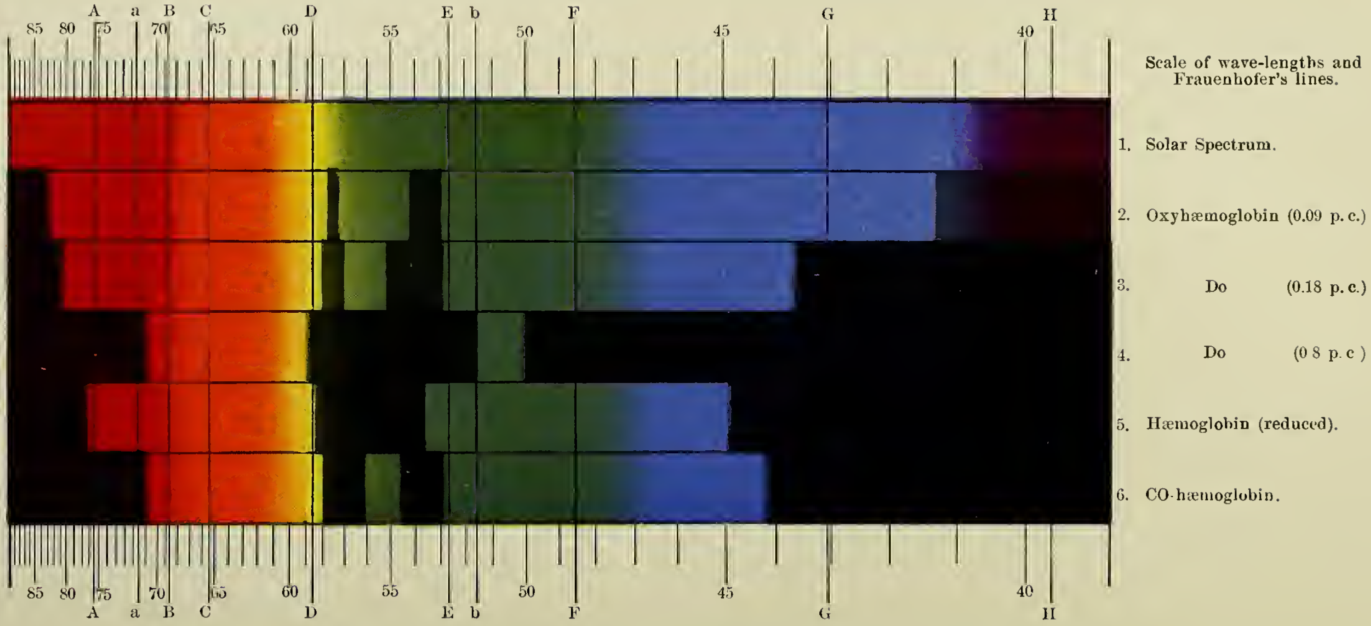
The quantitative determination of the degree of alkalinity of the blood becomes a matter of some clinical importance. The chemical composition of the blood is remarkably constant considering the complexity of its composition and the complexity of the processes involved in its rejuvenation and the complexity of the processes which free it of waste products. Through excess of inorganic salts in the food a temporary excess of those salts may exist in the blood; but the increased endosmosis of fluids and the increased excretion of urine and perspiration very soon carry off the excess of salts and water and restore equilibrium. Excess of fats and carbohydrates is deposited in the form of fat, thus restoring very readily the equilibrium in the blood, but leading eventually to an excess of fat deposit in the system.

Excess of proteids may be broken up, fats formed from the carbonaceous portion and deposited in that form. On the other hand a deficient supply of any of these may be for a short time overcome by the use of reserve materials; but sooner or later the deficiency will manifest itself in various disturbances of the general nutrition. Experience has proven that that constituent of the blood most important, from a clinical standpoint, is the hæmoglobin. The only function of hæmoglobin is to transfer oxygen *from the lungs*—the seat of external respiration,—*to the cells,*—the seat of internal respiration; and though the plasma assists in this function it is quite insufficient alone and in fact a small decrease in the hæmoglobin is soon attended by a disturbance in general nutrition through lack of a proper supply of oxygen to the active cells, *i. e.*, cells of secretion and excretion as well as muscle and nerve cells. Moreover, the important part that iron plays in the functions of hæmoglobin, the great difficulty with which iron is assimilated, together with the important proteid constituents of hæmoglobin make that compound a most sensitive and reliable index of the general nutrition both as to organic and inorganic compounds. It is, then, a matter of the greatest clinical importance to be able to determine with reasonable accuracy the amount of hæmoglobin present in the blood.

b. Quantitative Determination of Hæmoglobin.

1. **Dry Hæmoglobin** contains about 0.42 per cent. of Fe. All the iron of the blood is in the hæmoglobin. It therefore follows that the quantity of the iron in the ash of a weighed quantity of blood is an exact index of the quantity of hæmoglobin present. This method is very valuable for certain physiological investiga-

PLATE III.



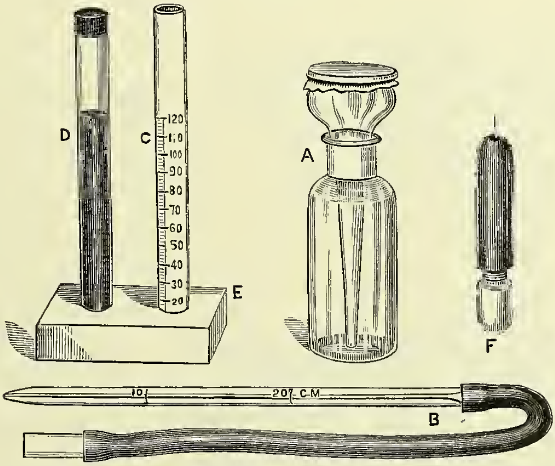
Showing Spectra of Hæmoglobin in certain qualitative and quantitative variations.

[After Schaefer. Text-book of Physiology, Vol. 1, p. 208.]

tions, but the time required to make a quantitative estimation of the iron is too great to justify this method for clinical use.

2. (*a*) IT HAS BEEN FOUND THAT SUNLIGHT or lamplight in passing through diluted blood before entering the slit of a *spectroscope* suffers an absorption of a part of the yellow and a part of the green of the spectrum; and the latter appears with two black bands through those colors—one just at the right of the D lines and a broader one just at the left of the E line (Plate III.). It has been further discovered that a quantitative variation of the hæmoglobin causes a broadening of these bands. Preyer has used this as a basis for a quantitative determination for clinical purposes. The accompanying Plate shows, in spectra 2, 3 and 4, the influence of a varying quantity of hæmoglobin upon the transmission of light by the prisms. An 0.8 per cent. solution of hæmoglobin absorbs most of the light, while a solution one-tenth that strength would absorb little light; namely, the two extremes of red and violet and two characteristic bands in the yellow and green. Study carefully the location and width of these absorption bands.

FIG. 90.



Gower's hæmoglobinometer. A, pipette bottle for distilled water; B, capillary pipette; C, graduate tube; D, tube with standard dilution; F, lancet for pricking the finger. (CHAPMAN.)

(*b*) A VARIATION OF THIS METHOD which gives much more exact results is described in Long's Chemical Physiology (pp. 150 to 156). In this method the *spectroscope* is converted into a *spectrophotometer* and the quantity of light transmitted is measured. The basis of the determination being the fact that equal dilutions of hæmoglobin transmit equal amounts of light.

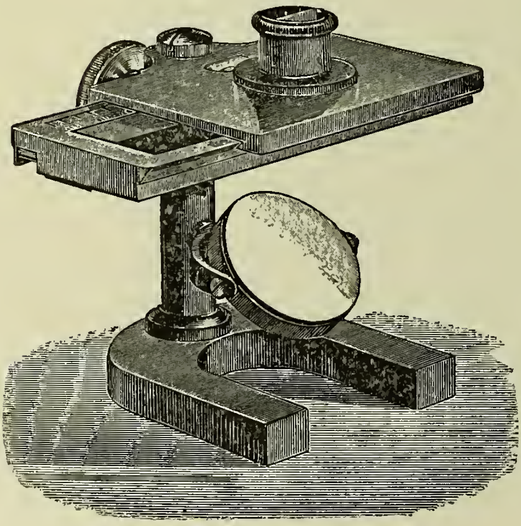
3. Colorimetric Methods of Determining the Hæmoglobin.

(*a*) The Hæmatinometer consists of two glass cells with parallel sides 1 cm. apart. One cell contains a known dilution of hæmoglobin [or of picrocarminate of ammonium] as a standard. In the other cell a measured quantity of blood is diluted with a measured quantity of H_2O until its color is the same as the standard solution, the per cent. quantity in the second cell would be the same then as in the first or standard cell and the degree of dilution being known the quantity of hæmoglobin in the blood tested may be easily computed.

(*b*) Gower's Hæmoglobinometer (see Fig. 90). The principle here is exactly the same as in the above; but the apparatus is very compact and the quantity of blood necessary for a test is only 20 cubic millimeters. The instrument is, therefore, much better adapted to clinical purposes than is the hæmatinometer.

(*c*) Fleischl's Hæmometer (see Fig. 91). This instrument is similar in principle though the standard solution is here represented by a plate of colored glass. The advantages of the instrument are that it is compact and portable and requires only a few (5–10) cubic millimeters of blood; it has, however, the disadvantages that the examinations must be made by lamp- or gaslight, and the range of error in reading is very wide, the reading by two individuals frequently differing by as much as 10 per cent.

Fig. 91.



Fleischl's hæmometer.

IV. FUNCTIONS OF THE VARIOUS PARTS OF THE BLOOD.

a. Plasma.

This part of the blood carries in liquid form the nutriment of the body. The nutriment enters the alimentary canal in the form of various liquid or solid proteids, carbohydrates, and fats, with salts, solid or in solution in water. During digestion the proteids are changed to peptones, the carbohydrates to soluble sugars, the fats to fatty acids and soaps; and the salts are dissolved so that the nutriment absorbed is much more uniform in both physical and chemical properties than was the food.

During absorption the peptones are changed to serum globulin and serum albumin, the fatty acids and soaps are changed to emulsions. Soon after absorption the sugars are deposited as glycogen in the liver or consumed in the muscles, the fats are likewise disposed so that the plasma is kept fairly uniform in the quality of its nutriment. Its functions are: (I) to carry absorbed nutriment to the metabolic tissues; (II) to carry excrement to the organs of excretion; (III) to assist in carrying oxygen to the tissues and in carrying CO_2 from tissues to lungs.

b. Corpuscles.

1. **The Red Blood Corpuscles.**—These modified cells are *oxygen carriers.* The oxygen is held chemically by the hæmoglobin and carried from the lung capillaries to the metabolic tissues where it is just as essential as the nutrients.

2. **The White Blood Corpuscles.**—(I) These cells carry solid particles from one part of the organism to another (see Decay and Destruction of Red Blood Corpuscles). (II) They fill breaks in the continuity of tissues and, with fibrin, build new tissue into the wound. (III) They surround foreign bodies (*e. g.*, slivers) protecting the tissues from extensive laceration and assisting the organism in throwing out the offending object by forming a minute abscess or "fester," which if not opened will usually break spontaneously, the sliver will be extruded and the opening close and heal spontaneously. In this complete process the leucocytes perform a most important part. (IV) The leucocytes "police" the organisms protecting it as far as possible from the invasion of pathogenic microbes. These are usually engulfed, digested by the leucocytes and expelled from the system. When conditions are unfavorable the leucocytes may not be able to successfully perform this service.

V. THE TOTAL QUANTITY OF THE BLOOD.

In cases of severe hemorrhage, where the quantity of blood lost can be more or less accurately determined, it may be important to know the total amount of blood in the body in order to estimate the proportion that has been lost. There are two methods for determining the total quantity of blood.

1. **The Determination in a Dead Animal.**—Welcker's (Zeitsch. f. rationale medicin, 1858) method is as follows: (I) Bleed the animal, taking the weight of the blood so obtained. (II) Of the blood first drawn, defibrinate a few grammes to dilute and use as a color standard. (III) Wash out the circulatory system with warm

normal saline solution, determining the blood by diluting the standard with a measured quantity of water to the same color. (IV) Remove and hash all tissues, making an aqueous extract, whose blood content may be determined as in (III). The sum of amounts (I), (III) and (IV) is the total. This varies somewhat for different animals; usually from $\frac{1}{12}$ to $\frac{1}{19}$ of the body weight, averaging $\frac{1}{13}$ in man and the dog, $\frac{1}{14}$ in the cat, $\frac{1}{19}$ in the rabbit and in the newborn child.

2. **The Determination in a Live Animal.**—This was accomplished by Gréhant and Quinquand (Jour. de l'anat. et physiol., etc., Paris, 1882, No. 6, p. 564), by allowing the animal to respire a known quantity of CO with oxygen, afterward determining the amount of CO in a small amount of drawn blood. Then, *Total blood: Drawn blood :: total CO: drawn CO.*

V. THE PROTECTION OF THE BLOOD SUPPLY.

If the blood plays such an important part in the economy of the body, may we not expect that some provision is made for the protection of animals, in a measure at least, from accidental breaks in the integrity of the system of tubes in which the blood circulates? If any slight accident may sever an artery from which the blood can flow unhindered, then surely would animal life be precarious. But there have arisen in the animal kingdom two methods of protection against the accident indicated above.

a. Location of the Vessels.

All important vessels are located very deeply. The somewhat superficial position of the human femoral artery in the upper part of the thigh, and of the axillary artery hold only for man since he assumed the erect posture; in the other mammals these arteries lie well protected behind the thigh and arm.

b. The Influence of the Intima.

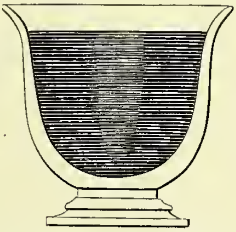
Many small vessels both veins and arteries lie near the surface of the body. What special provision is made for these? The inner coat of a severed small vessel either mechanically or by some ferment influence is a most important factor in the ready formation of a clot.

c. The Coagulation of the Blood.

The most important protection against excessive bleeding is the tendency of the blood to undergo a change as soon as it passes through a wound in a vessel. This remarkable change which the blood undergoes involves a chemical reaction between certain constituents of the blood; the wonderful feature about this reaction is the fact that normally it is *adjusted* in *time* and *place* to the severing of the continuity of a blood vessel.

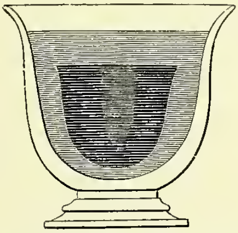
The principal gross phenomena of coagulation, as observed in a beaker of drawn blood, are: (I) the formation within two minutes of a jelly-like layer over the surface of the blood; (II) the formation of a similar layer, within two to seven minutes, around the sides of the vessel; (III) the formation of a complete homogeneous clot in from seven to sixteen minutes (see Fig. 92); (IV) the contraction of the clot, which results in the exudation of serum from its surface. Eventually the contraction is so extensive that the clot occupies about one-half of the entire volume, and usually rests upon the bottom of the dish (see Fig. 93). *The time required* to completely coagulate the blood to a condition shown in Fig. 93 is in man 2–16 min., in the horse 5–13 min., in the dog $\frac{1}{2}$–3 min., in the rabbit $\frac{1}{2}$–$1\frac{1}{2}$ min. In the pigeon the coagulation is almost instantaneous.

FIG. 92.



Bowl of recently coagulated blood, showing the whole mass uniformly solidified. (DALTON.)

FIG. 93.



Bowl of coagulated blood, after twelve hours; showing the clot contracted and floating in the fluid serum. (DALTON.)

Coagulation is hastened by: (I) temperature above normal body temperature; (II) contact with foreign matter; (III) agitation; (IV) addition of calcium salts.

Coagulation is retarded or prevented by: (I) low temperature; (II) addition of an equal volume of saturated solution of $MgSO_4$ or Na_2SO_4; (III) addition of oxalates, which precipitate the calcium as an oxalate; (IV) addition of leech extract; (V) injection of solution of commercial peptones into the vascular system of an animal before an experiment will retard coagulation. These are some of the questions which have presented themselves for solution, in this connection:

(1) What constituents of the blood take part in the reaction?

(2) Whence are these constituents derived?

(3) What are the factors which determine the time and place of coagulation?

All of these questions have been variously answered by various investigators. A review of the history of this investigation would consume too much time. Of the long list of students of these questions the name of Alexander Schmidt, who for over thirty years, has been experimenting in this field at the, Physiological Laboratory of Dorpat University, Russia, stands in the front rank. The Swedish investigator Hammarsten stands next in rank to Schmidt in this field. Alexander Schmidt's original theory published in 1861 was: *Fibrinogen, Fibrinoplastin* and *Fibrin Ferment* are the three fibrin factors and their combination is determined in time and place by the liberation of the ferment at the point of rupture of the endothelial lining of the blood vessels from leucocytes and endothelial plates. Hammarsten and Schmidt have more recently found that fibrinoplastin is not a necessary factor. Hammersten and the Dorpat School have further found that, " unless a certain amount of salts be present coagulation takes place slowly or only partially." Freund has shown that, " the process of coagulation is always accompanied by an excretion [separation] of phosphates of the alkaline earths. [1] Fibrin contains a constant amount of these phosphates. Coagulable fluids coagulate after the addition of these salts. This is true too of sulphates of these metals, *e. g.*, $CaSO_4$." The theory of Wooldridge deserves mention here only to afford an opportunity to quote Halliburton's statement regarding it: " 1. The whole theory is based upon experiments with peptone-plasma ; but such plasma performs differently from normal plasma. 2. It is difficult from Wooldridge's publications to find a logical basis for his conclusions." This statement was made ten years subsequent to the publication of the theory. Hammarsten's theory published in 1891 is, briefly stated, as follows : Coagulation is caused by *Fibrinogen* and Fibrin Ferment in the presence of neutral salts of the alkaline earths, especially $CaSO_4$ and $CaHPO_4$.

To Alexander Schmidt and the Dorpat School we must give the credit of making the most profound investigation of this subject. Most writers do Schmidt the injustice of only associating his name with the first theory which he published in the first years of his work, wholly ignoring all his subsequent investigations and the subsequent recasting of his theory. His publication in 1892 on *Blut lehre* is the most comprehensive treatise ever published on coagulation. Every step of the theory is based upon repeated experiment upon perfectly normal blood. Schmidt emphasizes the fact that coagulation is brought about by the action of a *ferment* upon the *fibrinogen ;* both of which exist in the blood. He further emphasizes the necessity of the presence of the calcium salts. His investigation, however, does not stop at this point; he and his pupils have sought the source of the fibrin-factors and find that not in the blood-corpuscles, not in the blood platelets and not in the endothelial cells alone is found the source of fibrin ferment but that it arises wherever protoplasm undergoes destructive metabolism ; and concludes finally : “ Fibrin-ferment is present in the free state not only in circulating blood in small quantities but also in small quantities is widely distributed throughout the entire organism.” He finds by experiment that it is less active in circulating blood than in freshly shed blood and determines the cause to be a rapid chemical change which takes place in the ferment immediately after the blood is shed. He calls the more active form *Thrombin* and the less active form in circulation *Pro-thrombin.* Further he and others find that it is a *nucleo-albumin* derived from the katabolism of the nucleus. As to *Fibrinogen:* he has also found that widely disseminated and has traced it back as a derivative from *Paraglobulin*, this in turn is derived from *Preglobulin*, and this from *cytoglobulin* which is a derivative of cell protoplasm or *cytoplasm.* The relation of these products to cell protoplasm on the one hand and to coagulation on the other is shown in the following diagram.

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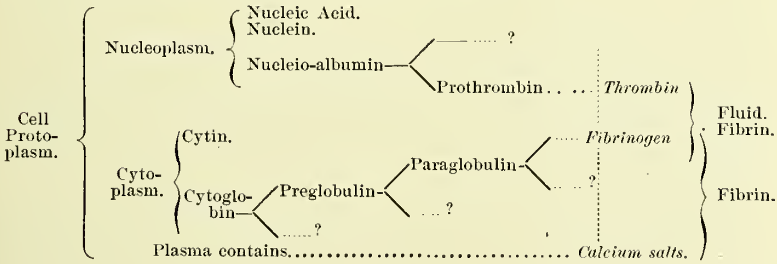
[1] The alkaline earths are Ca, Sr and Ba. The blood contains calcium phosphate.



Pekelharing's theory must be mentioned here. Briefly stated it is as follows : *Thrombin differs from nucleio-albumin in its richness in calcium salts. Fibrin contains much calcium. Fibrin is probably a calcium compound of fibrinogen. In coagulation the calcium salt is probably dissociated from fibrin ferment and associated with fibrinogen precipitating the latter in fine threads.* The difficulty with this theory is that it seems either to necessitate a quantitative relation between the amount of fibrin-ferment and the amount of fibrin precipitated, or to make the thrombin a carrier of the calcium, in which case we would have to answer some puzzling questions as to where and how the changes occur. But the investigators in this field uniformly give the quantity of ferment as minute, and ascribe to it a real ferment action so that the small amount suffices to produce a considerable effect if the time be sufficient ; furthermore the calcium salts present in the plasma would seem to satisfy the conditions. All things considered the later theory of Schmidt and Hammersten is as satisfactory as any.

VI. THE EFFECT OF HEMORRHAGE.

Repeated experiment has shown that one-fourth or one-third of the blood may be drawn without causing serious symptoms, and about one-half without causing death. One-half the circulating blood is supposed to be practically the limit. Whether the withdrawal of blood shall be more or less dangerous to life depends upon several complicating factors:

(*a*) *The time* consumed in the withdrawal of the blood is an important factor. The experiments of Prevost and Dumas in 1823, and more recently those of Nasse, Vierordt and others, have shown that during a slow withdrawal the blood will be replenished from the lymph and plasma of the tissues and if the hemorrhage cover sufficient time much more than 5 per cent. of the body-weight may be withdrawn; *e. g.*, Tolmatscheff in 71 days drew from a dog blood equal in weight to 15 per cent. of the body-weight. It is clear that in this case the withdrawal was sufficiently slow to enable the corpuscle-making organs to actually replenish the corpuscular elements. In this way may be demonstrated the rate at which the blood may be replenished. When the hemorrhage takes place within a shorter period—as one hour—the plasma alone will be in part replenished so that the blood last drawn would be much poorer in corpuscles than the blood first drawn.

(*b*) *The circumstances* under which the hemorrhage takes place enters as a factor into the effect. For example, loss of a given quantity of blood from an animal under anæsthesia causes less disturbance of the system than the loss of the same quantity as a result of an accident. In the latter case *shock* enters in as a strong factor; in fact, it is much the stronger factor of the two.

VII. TRANSFUSION.

a. The Transfusion of Blood.

The first recorded transfusion of blood was attempted by Lower in 1665. He successfully made a direct tranfusion of blood from one dog to another directly after the latter had been bled to the death-limit. The measure of the success of the transfusion is the fact that the second dog lived and showed no serious sequelæ of the operation.

In 1667 Denis successfully transfused the blood of a lamb to the circulatory system of a man. Subsequent attempts gave such a large percentage of failure that it fell quite into disrepute in the medical profession until after a long series of experiments upon lower animals. These experiments—for the most part performed during this century and many of them recently—have demonstrated the following facts :—(I) The blood of the same species, or even of the same genus, may be *directly* transfused, but the danger of coagulation is very great. (II) The defibrinated blood of the same species or genus may be transfused (Indirect Transfusion), but the danger here rests in the introduction of a fluid which contains a very much larger percentage of thrombin than exists in normal blood; this excess of thrombin induces coagulation on the slightest provocation. The process of defibrination subjects the blood to the danger of introduction of particles of foreign matter—even bacteria.

All of these make the dangers of the transfusion of defibrinated blood too hazardous to be recognized by the medical profession as a solution of the question.

b. The Transfusion of an Artificial Serum.

It has been found that the most serious symptoms of rapid hemorrhage arise from *sudden* decrease of the amount of circulating fluid, together with a moderate *fall* of *blood-pressure;* thus the principal indication to fulfill is *to replenish the quantity* of *fluid* without reference to the corpuscles or to the nutritive elements of the plasma. The fluid introduced must be of such a character as to cause no disturbance of the system. Warm, sterilized normal salt solution ($NaCl$ 0.6 per cent.), injected either subcutaneously or into an exposed vein, has been successfully used in surgical and obstetrical cases.

A transfusion fluid most successfully used in Europe is according to the following formula :

℞.	Sugar	35
	$NaCl$	6
	$NaOH$	0.05
	H_2O dist. ad.	1000.00

The solution is filtered and sterilized and injected at blood-temperature.

Indications for Transfusion : (I) Dangerous hemorrhage injection of one of the above fluids. (II) CO poisoning indicates the immediate indirect transfusion of blood of the same species. If the collapse is not too far advanced revival is possible.

VIII. QUANTITATIVE AND QUALITATIVE VARIATIONS OF THE BLOOD.

a. Methods of Observation.

(α) Determination of the proportion of plasma and corpuscles by the use of the *hæmatokrit.*

(β) Determination of the number of red and of white corpuscles per cu. mm. blood, by the use of the Gower or Zeiss *hæmacytometer.*

(γ) Determination of the size of the red blood corpuscles by the use of a microscope provided with an *eyepiece micrometer.*

(δ) Determination of the number or presence of the various varieties of leucocytes by the aid of reagents, etc., for Ehrlich's method of staining.

(ε) Determination of the quantity of hæmoglobin, by the use of the hæmatinometer, the hæmoglobinometer, or the spectro-photometer.

b. Variations.

1. **Conditions of the Blood which depend upon Quantitative Variation of some or all of its Constituents.** (*a*) The Quantity of Blood as a Whole cannot readily be determined in the living animal, but marked increase or decrease may be determined clinically by symptoms or by the history.

(α) Increase of the blood as a whole (*Polyæmia* or *Plethora*), indicated by swollen veins, hard, full pulse, etc.

(β) Decrease of the blood as a whole (*Oligæmia vera* or *Anæmia*), indicated by paleness or even marked pallor of skin and especially of mucous surfaces, *e. g.*, lips, or conjunctiva.

The history is also a very important aid to diagnosis and prognosis.

(*b*) Changes in the Quantity of different constituents of the blood.

(α) Increase in plasma (*Hydræmia*), after sudden decrease of excretion of water, which may occur within physiological limits after a sudden change from hot to cold weather or wet weather.

(β) Decrease in plasma (*Oligæmia Sicca*), observed within physiological limits after copious perspiration, diuresis, or diarrhœa.

(γ) Increase in the relative number of red blood corpuscles (*Plethora polycythæmia*), likely to occur when such periodic hemorrhages as menstruation or nosebleed are suddenly stopped.

(δ) Decrease in the relative number of red blood corpuscles (*Anæmia vera*) or oligocythæmia.

(ε) Increase in the relative number of leucocytes, especially of the neutrophile variety of leucocytes. This may be moderate in extent and transitory (*leucocytosis*), or it may be excessive in extent and persistent, indicating a serious departure from the normal (*leucocythemia* or *leukæmiæ*).

2. **Conditions which Depend upon the Qualitative Variation of Constituents of the Blood.**—(*a*) Change in the quality of the plasma; containing too little nutriment or too much waste matter.

(β) Decrease in the hæmoglobin of the red blood corpuscles.

(γ) Increase in the size of the red blood corpuscles, or increase in the relative number of megaloblasts, associated with pernicious anæmia.

(δ) Decrease in the size of the red blood corpuscles or increase in the relative number of microblasts, associated with anæmia.

(ε) Presence of many red blood corpuscles of irregular size and shape, associated with pernicious anæmia.

2. THE LYMPH.

I. PHYSICAL PROPERTIES.

Like blood this liquid is composed of a plasma in which corpuscles float. The lymph plasma is quite like blood plasma in its composition and in its power to coagulate.

1. **Color.**—The lymph of the smaller lymphatics has a light yellowish color: That of the thoracic duct is yellowish opalescent or even milky. It assumes the latter color after a meal when it is laden with fat. In that condition it is usually called chyle.

2. The **Specific Gravity** of the lymph is 1012–1022.

II. THE MORPHOLOGY OF THE LYMPH.

The morphotic elements of the lymph are the *leucocytes*. (Quid vide.)

III. THE CHEMICAL PROPERTIES OF THE LYMPH.

CONSTITUENTS.	LYMPH OF MAN.	CHYLE OF DOG.
WATER.	94.2	90.67
SOLIDS.	4.8	9.33
Organic.	3.95	8.54
Proteids (Serum albumin, serum globulin, fibrin)............	3.75	2.21
Fats, Lecithin and Cholesterin..............................	0.10	6.10
Sugar	0.10	0.23
Inorganic.	0.85	0.79
Sodium chloride...	0.56	
Sodium carbonate......	0.24	
Other salts containing K, Ca, and traces of Mg and Fe as chlorides, sulphates or phosphates..........	0.05	

C. THE FORMATION AND DESTRUCTION OF THE CORPUSCLES.

1. THE ORIGIN OF THE RED BLOOD CORPUSCLES.

1. **During Intrauterine Life.**—The prenatal origin of the corpuscles may be subdivided into two periods: *the embryonic period*, and *the fœtal period.*

(*a*) The Embryonic Period is characterized by the formation of blood and blood vessels in the *vascular area* of the egg and of blood vessels within the embryo. In both cases the fundaments of the circulatory system are formed from mesenchyme cells. Regarding the primitive red blood corpuscles we should remember that they "exhibit amœboid movements, have less than the usual quantity of hæmoglobin, are nucleated, globular, larger and more irregular and variable than the permanent corpuscles." Next they become normally colored, but they retain the nucleus during intrauterine life. They are capable of multiplication by karyokinesis. The relative number of non-nucleated corpuscles rapidly increases during the fœtal period, in mammals, until at birth no nucleated corpuscles remain.

(*b*) The Fœtal Period. After the establishment of the different systems of organs the formation of blood corpuscles goes on within the embryo. Neumann and Löwit observed the formation of nucleated blood corpuscles in the fœtal *liver* and in the *spleen ;* while Foa and Saviola observed it in the lymphatic glands.

2. **During Extrauterine Life.**—"The balance of evidence points to the formation of red-blood corpuscles in extrauterine life—in all higher vertebrates—by the same process as in fœtal life, *i. e.*, by karyokinesis of a typical cellular element—the erythroblast—which, during extrauterine life, is chiefly found in the red marrow of bones." (Bizzozero, Neumann.) The transition from the fœtal method to the extrauterine method is not a sudden one, and the fœtal method may be later employed after severe hemorrhages.

2. DECAY OF THE RED BLOOD CORPUSCLES.

Investigation has revealed the following facts: (I) There are fewer red corpuscles in the hepatic vein than in the portal vein. (II) The bile pigments are formed from hæmoglobin. (III) Disintegrated red corpuscles are to be seen in the cells of the spleen pulp. The conclusions to be drawn from these facts are: (I) The corpuscles in question meet their end in the *liver* and *spleen.* (II) At least a part of the hæmoglobin is lost in the excretion of the bile pigments. Further investigation shows that a part of the disintegrated corpuscles is taken up by the leucocytes and carried to the red marrow of bones—possibly to the spleen, and, in the former location at least, utilized by the erythroblasts in building up new corpuscles. It is estimated that the life of a red blood corpuscle is about three or four weeks.

3. THE FORMATION AND DESTRUCTION OF LEUCOCYTES.

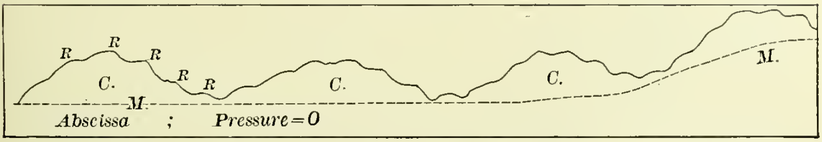
The leucocytes are formed chiefly as lymph corpuscles in the lymphatic glands. The fine meshed adenoid tissue of these glands seems to catch and hold all of the senile leucocytes and to allow only the more active corpuscles to pass through. Although many leucocytes are stopped by the lymphatic glands, there are very many more in the efferent than in the afferent stream. The necessary inference is that the lymph gland forms these new leucocytes and they enter the lymph stream and so pass into the circulation.

What has been observed in the relation of the lymphatic glands holds for the spleen, one of whose functions seems to be to detain the leucocytes which have engulfed senile red blood corpuscles. In some way the broken down red corpuscle is transferred to the liver, probably through the agency of the leucocytes. The splenic vein contains far more leucocytes than the splenic artery. The spleen must be a nidus for their formation.

4. SUMMARY OF THE FUNCTIONS OF THE SPLEEN.

The spleen is as completely and exclusively connected with the circulatory system as is the heart. The general function of the spleen seems to be to keep the corpuscular elements of the blood constant, or at least to assist in that important office.

FIG. 94.



R R = Respiratory waves ; *C C C*, waves of rhythmical contraction of muscle tissue of capsule and trabeculæ ; *M M* = wave occurring 4–5 hours after a meal. Waves *R R* evidently depend upon general blood-pressure. Heart waves do not show in the oncometer curve. The waves *C C* probably show an independent action of the spleen directed to the partial emptying out of its blood. The wave *M* is probably caused by a heaping up of absorbed food-stuffs.

The specific functions of the spleen are obscure. Some idea of its functions may be gained by the following methods:

(*a*) BY EXTIRPATION.—The removal of a dog's spleen seems to make no essential difference in his general physical condition. After a few weeks an enlargement of the lymph glands and an increase of the red marrow of the long bones occur.

(*b*) By Chemical Examination it is found, 1st, that the spleen yields a preponderance of those inorganic salts found in the red blood corpuscles; 2d, that the extractives are such as are produced by the breaking up of proteids.

Fig. 95.

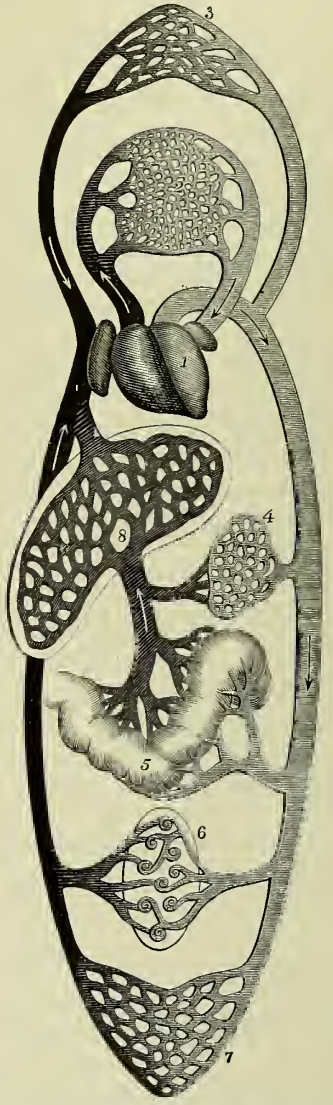


Diagram of the circulation. 1, heart; 2, lungs. 3, head and upper extremities; 4, spleen; 5, intestine; 6, kidney; 7, lower extremities; 8, liver. (Dalton.)

(*c*) By Microscopic Examination after Hemorrhage.—The spleen normally contains large leucocytes which have taken in one or more red blood corpuscles, but after hemorrhage also numerous red nucleated hematoblasts (homologues to the erythroblasts of red marrow of bones).

(*d*) By Oncometer Curves. (See Fig. 94.)—An oncometer is a metallic case made for the purpose of enclosing an active organ. The space between the organ and the case is filled with warm saline solution. Any change in the volume of the organ affects the recording apparatus by transmission through a column of liquid which is continuous with that which surrounds the organ.

D. THE CIRCULATION OF THE FLUIDS.

The best general idea of the course which the blood takes in its circuit through the body may be gotten from such a schema as that shown in the accompanying figure 59.

1. THE ACTION OF THE HEART.

In order to observe directly the movements of the heart one may institute artificial respiration, open the chest, tying all bleeding vessels, open the pericardium, and note at leisure the movements of the organ while it works under the slightly changed conditions.

In such an experiment one may observe: (1) A series of contractions (systole) alternating with a series of dilatations (diastole).

(II) Auricular contraction precedes ventricular contraction. (III) Auricular contraction begins with the contraction of the muscle fibers which encircle the large veins, immediately thereupon involving the whole auricular wall. (IV) The auricles contract simultaneously, but are not completely emptied by the beginning of ventricular contraction. (V) Auricular systole ends at the moment that ventricular systole begins. (VI) The ventricles begin their contraction simultaneously and cease simultaneously.

a. Changes of Form which the Heart Undergoes.

(*a*) OBSERVED IN THE OPEN THORAX of a mammal, which is lying upon its back.

(*α*) During diastole the transverse diameter becomes markedly greater and the dorso-ventral diameter less than in systole giving an elliptical outline.

(*β*) During systole the transverse diameter becomes shorter and the dorso-ventral longer, approaching a circle in outline. The three factors which work together to produce this change are: (I) The intra-ventricular change of pressure; (II) the force of gravitation; (III) the atmospheric pressure.

(*b*) OBSERVED IN THE CLOSED THORAX of a mammal by the use of needles passed through the thoracic wall into the heart wall at different angles and locations. For the following facts we are indebted to Haycraft:

(*α*) During diastole the heart hangs passive in its pericardium, suspended by its connection with the great vessels which enter or leave its base. While filling all of its dimensions increase, though the lateral diameter may increase somewhat more than the dorso-ventral, owing to the bulging out on the right side of the flaccid right ventricular wall.

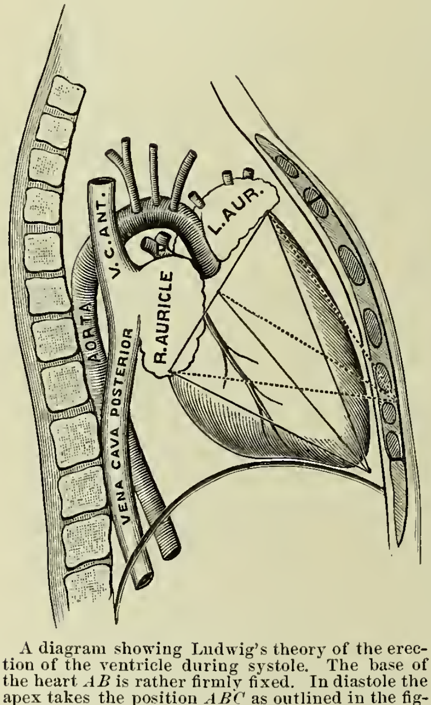
(*β*) During systole all of the dimensions of the heart decrease but any increase of lateral over dorso-ventral dimension is compensated during systole so that the cross section of the heart at the end of systole presents nearly a circular outline. The *antero-posterior dimensions*, or the distance between base and apex, also decreases, but the apex is not in consequence drawn away from the chest wall. The reason for this will be discussed under the next topic.

b. Changes of Position of the Heart Incident to its Activity.

1. **Mechanical Factors which Tend to Produce a Change in the Position of the Heart.**—(*α*) *The Asymmetrical Position* which the apex takes during diastole; either (I) because of the action of gravity in the dorsal position, or (II) because of the contact with the chest wall in the normal position. (*β*) The first

factor together with the fact that whenever the pressure increases within a liquid-filled sack, the latter *tends to erect* and stand in such a position that the tension on each part of the wall shall be equal. A condition of *pressure-* and *tension-equilibrium*, of closed cavities. (γ) Whenever a closed receptacle ejects its contents through action of a force mechanically within itself, the structure *undergoes a recoil* in obedience to Newton's law of motion that "action and reaction are equal in opposite directions." (δ) *The base of the heart is relatively firmly fixed;* the vertebral column forming the basis of fixation, the large vessels being held well in place by strong connective tissue attachments. Besides this the arch of the aorta passes over the root of the left lung, while the pulmonary artery passes directly into the root of both lungs.

Fig. 96.



A diagram showing Ludwig's theory of the erection of the ventricle during systole. The base of the heart *AB* is rather firmly fixed. In diastole the apex takes the position *ABC* as outlined in the figure. In systole it tends to erect by intra-ventricular pressure and stand in the position *ABC′*.

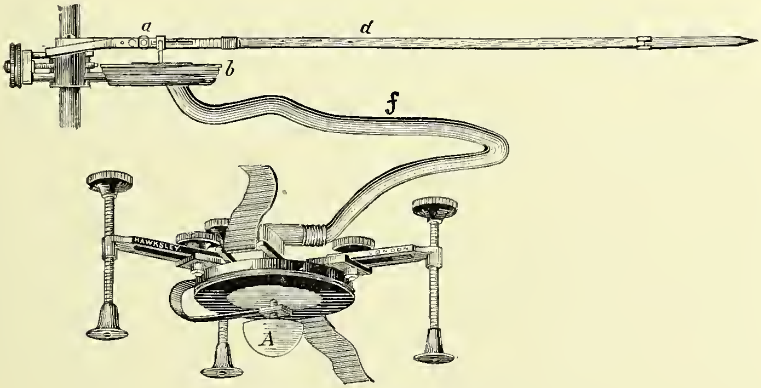
2. **The Influence of the Enumerated Factors upon the Action of the Heart.**—(*a*) The Sudden Rise of Intra-ventricular Pressure During Auricular Systole would have two tendencies: (I) To cause the apex to assume a more symmetrical position with respect to the base, *i. e.*, to give the apex an impulse against the chest wall; (II) the light auricles would tend to recoil strongly, but this would be largely counteracted by tissues above the auricles, as well as by the weight of the columns of blood in the vena cava anterior and the pulmonary veins.

(*b*) The Great Rise in Intra-ventricular Pressure During Ventricular Systole gives the apex a sudden and strong impulse toward the point of symmetry, *i. e.*, toward the thoracic wall just at the beginning of ventricular systole (see Fig. 96). After the position of symmetry has been assumed there will be a tendency for either a sustained crest or for a gradual fall, the latter owing to a decrease in the dimensions of the ventricle and not to a falling from the position of symmetry.

(*c*) THERE WILL BE A RECOIL OF THE HEART when the contents of the ventricular cavity are ejected into the arteries; but the direction of recoil is at nearly right angles with the direction of the movement of the apex when coming into the position of symmetry, *i. e.*, the direction of recoil is in the line determined approximately by the axis of the left ventricle.

Observation of the heart in the closed thorax may be made with a *cardiograph.* This instrument, shown in Fig. 97, consists of a pair of Marey tambours. The receiving tambour is provided with a button *A*, which is placed over the site of the apex beat of the heart. Movements of the button affect directly the membrane of the receiving tambour. Through the connecting tube, *f*, movements of the receiving tambour are transmitted to the recording tambour, *b*, whose membrane supports the recording lever, *d*. The tracing point of this lever may be brought into contact with a kymograph drum and a permanent and exact record made of the movements of the thoracic wall produced by the apex beat of the heart.

FIG. 97.

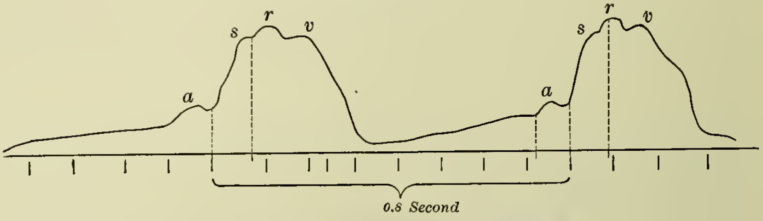


The cardiograph. (CHAPMAN.)

From what has been said regarding the relative influence of the erection and the recoil of the ventricle it is evident that the recoil will variously affect the cardiogram according to the position of the subject under observation. Furthermore the force of the recoil will be broken by just that factor which emphasizes the action of heart in assuming a symmetrical position, namely the fixing of the base of the heart. The recoil affects the cardiogram in different ways, if it appears at all. If there is only one superimposed wave beyond the systolic rise that one wave may be taken to represent the effect of the closure of the semilunar valves, unless it is within *0.1* of a *second from* the *beginning* of the *systolic wave.*

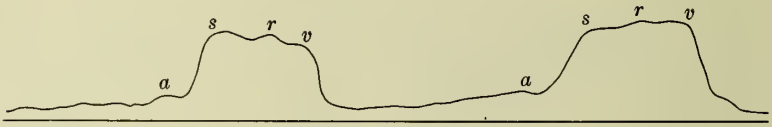
Any wave between the systolic wave crest and the semilunar wave may be taken as the recoil wave. Especially strong is the evidence favoring that interpretation, provided the wave in question falls between 0.05 second and 0.1 second after the beginning of the systolic wave. Should the cardiogram present other small superimposed crests they may be interpreted as *instrumental, i. e.,* formed by secondary vibrations of the membranes or of the elastic media of transmission. (See Figs. 98, 99, 100, 101.)

Fig. 98.



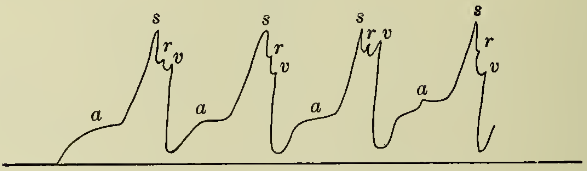
Cardiogram taken by Chauveau and Marey. *a* = Auricle wave; *s* = Systolic rise; *r* = Recoil wave; *v* = Valvular wave.

Fig. 99.



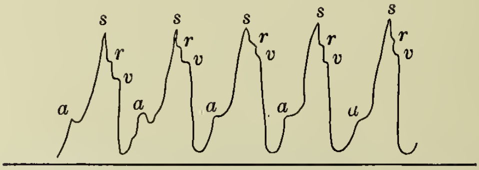
Cardiogram taken by Edgren.

Fig. 100.



Cardiogram taken by Sanderson, with fast drum.

Fig. 101.



Cardiogram taken at the Physiological Laboratory of the Northwestern University Medical School.

c. Changes of Pressure Within the Heart Incident to Its Activities.

Intra-Ventricular Pressure.

The strong contractions of the muscle tissue of the walls of the heart *cause* the cavity of the ventricle to be decreased in volume during systole; while the relaxation *permits* the increase of the volume of the ventricular cavity during diastole. This cavity is constantly filled with blood. At the beginning of systole there is about 180 c.c. of blood in each ventricle; at the end of systole the ventricles are practically empty. The contraction of the ventricles subjects the liquid contents to sufficient pressure to eject it into the aorta and pulmonary artery. Liquids flow from a point of higher pressure to a point of lower pressure. The pressure in the arteries named must be sufficient to overcome all resistance beyond, otherwise the blood could not flow out of them through the capillaries and into the veins. The pressure in the ventricles, in turn, must be higher than the pressure in the large arteries, otherwise the blood could not flow from the ventricles into the arteries. The pressure necessary to force the blood out of the ventricles is produced by the contraction of the ventricular walls upon the ventricular contents. The ventricle is then a *force-pump.*

The ancients, from Aristotle to and including Galen, believed the heart to be a *suction-pipe.* They thought that the ventricles actively dilated, drawing the blood in; then actively contracted, forcing it out. (See Historical Introduction to the Circulation.) Harvey showed that the dilatation of the ventricles is passive, and that only the contraction is active.

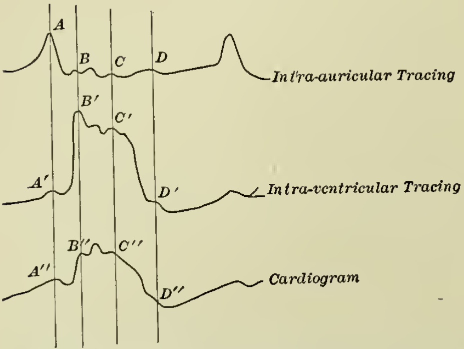
The question of intra-ventricular pressure has been a much debated one for a long period.

Physiologists have endeavored to determine not only the range of variation of pressure within the ventricles, but also the variations of pressure which occur between the maximum and the minimum; in other words, to determine the qualitative as well as the quantitative changes of pressure.

Three different devices have been contrived for this purpose. Chauveau and Marey used a modification of the Marey tambours. The recording tambour having the usual contraction but the receiving tambour was a small inflated rubber bulb. A double-lumened tube, bearing one bulb at its end, connected with one lumen and another bulb a few centimeters above the end, connected with the other lumen, was joined to two recording tambours, one communicating with each bulb. The tube was introduced, through the jugular vein, into the right side of the heart. The bulbs were so located that the end bulb passed into the cavity of the right ventricle while the other one reached to the auricular cavity. A third pair of tambours was arranged to record the movements of the apex of the heart. In this way three synchronous tracings were recorded: variations of the *intra-auricular pressure*, variations of the *intra-ventricular pressure* and *cardiogram* (see Fig. 102).

These tracings make it evident: (I) that auricular pressure reaches a maximum before ventricular pressure begins; (II) that during high ventricular pressure the auricular pressure is at a minimum. This method, however, gives only qualitative changes, and is subject to errors in its elastic transmission.

Fig. 102.



Intra-cardiac pressure tracings obtained by Chauveau and Marey. The vertical lines show the synchronous parts of the tracings. A, A', A'', effect of auricular systole; B, B', B'', effect of ventricular systole; C, C', C'', effect of closure of ventricular systole.

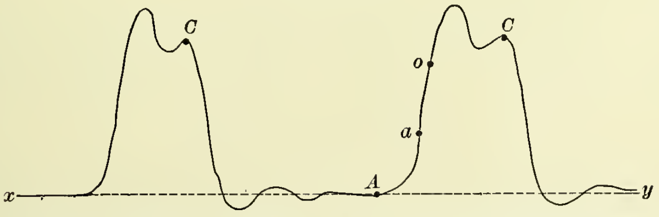
In 1878 Goltz and Gaule ("Ueber die Saugkraft des Herzens," Archiv f. d. ges. Physiol., Bd. XVII., S. 100) used a new technique. They devised a mercury manometer provided with a reversible valve. Turned in one direction the manometer records only maximum pressures, reversed it records only minimum pressures. This manometer was put into communication with the ventricular cavities through an inelastic connecting tube introduced along a blood vessel into the cavity to be tested. This method showed a maximum (left) *intra-ventricular* pressure of 176 to 234 mm. of mercury; a minimum pressure of — 30 mm. to — 38 mm. of mercury. In the right ventricle the maximum was 26 to 72 mm.; the minimum was — 8 to — 25 mm. In every experiment the maximum pressure in the left ventricle was 18 to 22 mm. greater than the maximum aortic pressure. Note that the minimum pressure is less than atmospheric pressure. That seems to justify the conclusion that the ventricle exerts a suction equal to 30 to 38 mm. of mercury. In this connection we must not forget that the heart is inclosed in a sealed cavity whose pressure is usually negative, though this negative pressure is greater during inspiration than during expiration. If a minimum manometer be introduced into the thorax the mercury will fall from 9 to 40 mm. according to the character of the respiration, 9 in quiet inspiration and 30 to 40 in forced inspiration. In any particular observation the manometer registers the lowest pressure reached in any inspiration made by the animal during the observation. If the manometer tube be passed on into the ventricle it will register the lowest pressure reached in any diastole during the experiment.

If the *intra-ventricular* is no lower than the intra-thoracic pressure there could be no suction of the blood from the thoracic vessels or auricles into the heart. The figures given above for intra-ventricular pressure and intra-thoracic pressure indicate that there may or may not be a slight suction upon the thoracic blood. In quiet breathing one would expect the negative pressure of the ventricle to exceed that of the thorax by about 20 mm. stand of mercury.

In 1894 Professor Gaule, lecturing before his students in the University of Zurich, said in this connection, "At the beginning of diastole any occurrence of negative intra-ventricular pressure is to be attributed to the sudden widening of the base of the aorta on the closure of the semilunar valves, thus suddenly opening the upper end of the ventricular cavity."

A third method of recording the variations of intra-ventricular pressure has been elaborated by Rolleston. His instrument consists of a delicate brass cylinder with hard-rubber piston. The piston receives the pressure of the atmosphere upon one side and that of the blood upon the other,—the blood-pressure being transmitted to the cylinder through a long trochar introduced into the ventricular cavity. The piston in turn moves a writing lever whose rise and fall is controlled by the resistance to torsion of a steel ribbon. This apparatus has the great advantage of showing not only qualitative but quantitative changes of pressure, for the value of the steel spring may be determined in advance. "Rolleston's conclusions are as follows: (I) There is no distinct and separate auricular contraction marked in the curves obtained from either right or left ventricles, the auricular and ventricular rises of pressure being merged into one continuous rise. (II) The auriculo-ventricular valves are closed before any great rise of pressure within the ventricle above that which results from the

FIG. 103.



Curve from left ventricle. (ROLLESTON.) *xy*, Zero line, or atmospheric pressure; *A*, part of curve due to intra-auricular pressure; *a*, auriculo-ventricular valves close; *o*, semilunar valves open; *C*, semi-lunar valves close; *CA*, period of ventricular diastole.

auricular systole. (III) The semilunar valves open at the point situated about the junction of the middle and upper thirds of the ascending limb of the curve (*o*) and the closure about the beginning of the descending limb (*c*). (IV) The minimum pressure in the ventricle MAY fall below that of the atmosphere but the amount varies considerably. (Rolleston, quoted by Halliburton, Handbook, p. 420.) (See Fig. 103.)

The facts regarding the changes of intra-cardiac pressure may be summed up as follows :

(*a*) The active work of the auricle is accomplished in its systole, which drives into the ventricle the blood which it has received from the veins. The thin-walled auricle, in common with the thin-walled veins, expands, under the negative intra-thoracic pressure, to receive the venous blood which rushes into the thorax during inspiration. The structure of the auricles is such that the pressure within them can never fall below that of the thorax in general.

(*b*) The active work of the ventricle is accomplished in its systole, which drives into the arteries the blood which it has received from the auricle.

(*c*) Passively the walls of the ventricle will be dilated by the negative intra-thoracic pressure, but the pressure within the ventricle could, by this cause, never exceed (negatively) the negative pressure of the thorax. But the negative pressure of the ventricle frequently does exceed the negative pressure of the cavity which contains it. There are two ways to account for this :

(*α*) The natural position of absolute relaxation does not completely close the ventricular cavity. The active contraction of systole carries the walls beyond this position of absolute relaxation in order to completely empty the ventricle. At the end of systole the walls spring back by their natural elasticity to the position of absolute relaxation, thus exerting a momentary negative pressure beyond that of the surrounding thorax.

(*β*) The sudden expansion of the upper part of the ventricle by the widening aorta, as suggested by Gaule, has been mentioned above. But in these changes the walls of the ventricle are absolutely passive.

d. **The Cardiac Cycle.**

The term *cardiac cycle* has been applied to the ever-recurring series of events which are repeated about once every second in the human heart. Briefly rehearsed, these events are : (I) *The auricular systole,* which empties the auricle and fills the ventricle, and which ends with the closure of the auriculo-ventricular valves. (II) *The ventricular systole,* which empties the ventricle into the artery through the forced semilunar valves. During the ventric-

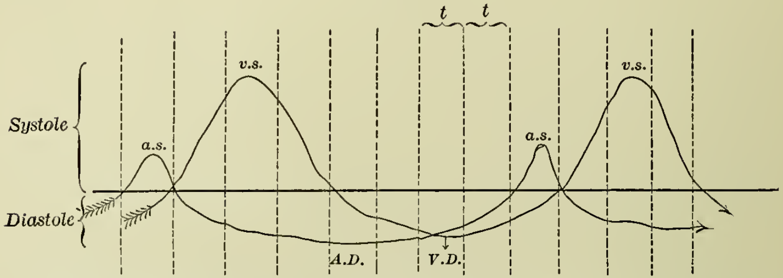
1. Events of the Cardiac Cycle.—Tabulated.

THE CARDIAC CYCLE.

EVENT.	CONDITION OF		FORCE INVOLVED.	WAYS POSSIBLE.		WAYS DETERMINED.		CONDITION OF	
	VENTRICLE AT BEGINNING.	AURICLE AT BEGINNING.		I.	II.	I.	II.	AURICLE AT END.	VENTRICLE AT END.
1 Auricular Systole.	Empty.	Full.	Contraction of Auricular Walls.	To Ventricle.	To Veins.	OPEN to Ventricle by Relaxation of Walls and Opening of Valves.	BLOCKED to veins by Counter Pressure and Contraction of Veins.	Empty.	Full.
—	—	—	—	—	—	—	—	—	—
2 Ventricular Systole.	Full.	Empty or Filling.	Contraction of Ventricular Walls.	To Arteries.	To Auricle.	OPEN to arteries by Lower Pressure and Opening Valves.	BLOCKED to Auricle by the Auriculo-ventricular Valves.	Filling.	Empty.
—	—	—	—	—	—	—	—	—	—
3 Rest or Diastole.	Empty.	Filling.	Aspiration of Thorax, Elasticity of Lungs, Muscular Contractions, etc., etc.	To Auricle.	To Ventricle.	OPEN to Auricle by Lower Pressure.	OPEN to Ventricle by Lower Pressure and Open Valve.	Full.	Filling.

ular systole the auricle is filling. (III) *Rest,* which includes all of the ventricular diastole and a little more than half of the auricular diastole. During the *rest period* blood is flowing freely into the auricle and through the auriculo-ventricular valve into the ventricle.

FIG. 104.



Time relations of heart cycle. $t = 0.1$ second of time; *a.s.* = auricular systole, 0.1 sec. *v.s.* = ventricular systole, 0.3 sec.; *V.D.* = veutricular diastole, 0.7 sec.; *A.D.* = auricular diastole, 0.5 sec. Total cardiac cycle, 0.8 sec.

The time of the average heart cycle in the human male adult is 0.8 second, which is distributed as follows:

The ventricular systole consumes 0.3 second; diastole, 0.5 second. The auricular systole consumes 0.1 second and the diastole 0.7 second. Heart systole, 0.4 second; heart diastole, 0.4 second. (See Fig. 104.)

e. The Work Done by the Heart.

1. **Data.**—(I) Maximum pressure in left ventricle varies between 140–200 mm. Hg. (II) The maximum pressure in right ventricle about 60 mm. Hg. (III) The amount of blood ejected against the above pressure varies, for the left [or right] ventricle from 120 to 180 c.c.

2. **To Derive a Special Formula for Work of Heart.**

Formula: Let W = work done.
" H = height in cm.
" g = weight in grammes.
" m = centimeters of Hg pressure.
" b = number c.c. of blood ejected at one systole.

Now a general formula for work done when the work is to be expressed in Gm.-cm. is: $W = g \times H$. To determine W, we have to first find the value of g and H. A pressure of m cm. of mercury would be equal to a pressure of $13.6\,m$ cm. of water and $\frac{13.6\,m}{1.055}$ cm. of blood. The work done in ejecting from the heart g grammes of blood against m cm. of mercury pressure would be the same as the work done in raising g gms. of blood to the height of $\frac{13.6\,m}{1.055}$ cm. Now what is the weight of b c.c. of blood? Naturally the volume times the specific gravity or $g = b \times 1.055$. The formula would therefore be:

$$W = \frac{b \times 1.055}{1} \times \frac{13.6 \times m}{1.055} \text{ or } W = 13.6\,bm.$$

3. **Problems.**—(*a*) How much does the left ventricle perform in each systole if 120 c.c. of blood is ejected against 14 cm. of pressure? $W = 13.6 \times 120 \times 14 = 22848$ gramme-centimeters. (*b*) How much work does the heart perform at each systole if the right ventricle expels the same quantity of blood against two-fifths as great pressure?

$$W = [13.6 \times 120 \times 14] + \left[13.6 \times 120 \times \frac{2 \times 14}{5}\right] \text{ or } \frac{7}{5} \text{ of}$$

work done by left ventricle alone = 31987 gramme-centimeters. (*c*) How much work will the heart do in 24 hours if it ejects 150 c.c. of blood into the arteries against 150 mm. of Hg pressure at the rate of 60 beats per minute. $W = 13.6 \times 15 \times 150 \times 60 \times 24 = 2{,}115{,}072{,}000$ gramme-centimeters. (*d*) If that represents the number of gramme-centimeters of work done by the heart of a man of 60 Ko. weight; how many meters would that amount of work lift his body vertically?

$$W = \frac{136 \times 15 \times 150 \times 60 \times 60 \times 24}{1000 \times 100 \times 60} = 352.5 \text{ meters.}$$

It would take about two hours of hard climbing for a man to lift his body through 350 meters; so that the heart can do about one-fourth as much work as all of those skeletal muscles involved in locomotion or, in fact, in manual labor.

f. The Sounds of the Heart.

1. **Character.**—There is a succession of two sounds separated by a pause—lūb-dŭp—lūb-dŭp, etc. The first sound (lūb) is longer in duration and lower in pitch than the second.

2. **Cause of the Heart-sounds.** (*a*) The First Sound.—It is synchronous with ventricular systole; it is therefore universally associated with the events which are taking place in the heart at the time: (I) Vigorous muscular contractions; (II) friction of blood rushing through the semilunar valves; (III) friction of surface of heart incident to its change of shape within the pericardium; (IV) friction of heart against neighboring structures in the thorax incident to its change of position in the thorax. As

any one of these four factors may be variously modified by various diseases, it is evident that a close study of the normal heart sounds is of great importance.

(*b*) THE SECOND SOUND of the heart is synchronous with the closure of the semilunar valves of the aorta and pulmonary artery, and as the quality of the sound is such as might readily be attributed to the closure of those valves, it is now quite generally interpreted in that way. The fact that a lesion of these valves makes a marked change in the quality of the second sound would seem to demonstrate conclusively that the closure of the semilunar valves is at least the most important factor in the second sound. The most advantageous position for hearing the first sound is at the apex, while the second sound is most easily heard over the base of the heart.

2. THE CIRCULATION OF THE BLOOD.

The problems of this field of physiology are physical problems, of the flow of liquids through tubes. As far as arterial circulation is concerned the phenomena are those *of the flow of liquids through elastic tubes under the influence of an intermittent initial force.* For the physical presentation of these problems see the physical introduction to this chapter.

a. The Circulation in the Arteries.

1. **Cause.**—There is one, and only one, cause for the flow of blood in the arteries; namely, *ventricular systole.* The high intraventricular pressure induced by the systolic contraction is transmitted to the large arterial trunks. The blood flows from the left ventricle to the aorta because the pressure is higher in the ventricle than in the aorta; it flows from the aorta into its branches because the pressure is higher in the aorta than in its branches, and so on, the energy of ventricular systole being gradually expended in overcoming resistance, so that the lateral pressure gradually decreases from the ventricle to the capillaries.

The initial energy is, however, not all expended in forcing the blood to and through the capillaries, so that there is still a small residuum of heart energy left when the blood enters the veins to assist other factors in returning the blood to the heart.

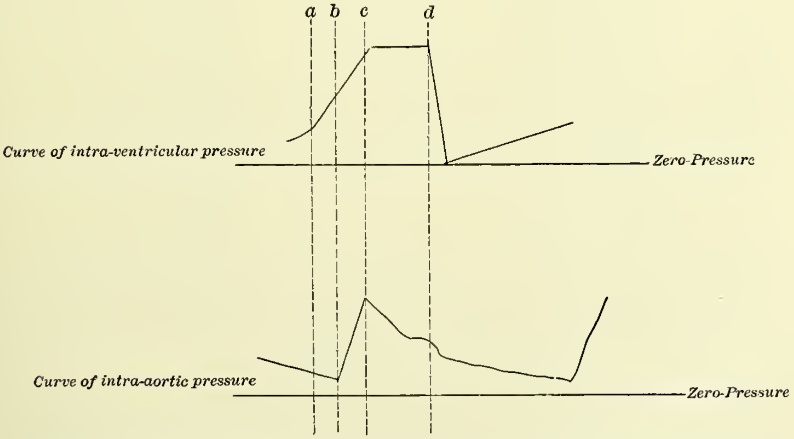
2. **Blood Pressure.** (*a*) METHODS OF DETERMINING.—The blood-pressure is usually determined by the use either of a mercurial manometer or of a spring manometer. The mercurial manometer was first used and modified for this purpose by Ludwig. His complete apparatus for measuring and recording the quantity and variations of blood-pressure consists of the mercurial manometer whose proximal limb is connected to the artery through

a lead or rubber tube and canula filled with a solution which will retard the coagulation of the blood. The distal limb is fitted with an ivory float which bears a tracing point. The complete manometer as described is fixed to a recording apparatus which consists of a rotating cylinder propelled by clock-work. Originally the whole apparatus was called a *kymographion* (wave-writer); later the term kymographion, shortened to kymograph, has been applied to the recording drum which is now extensively used in experimental physiology.

The spring manometer of Fick utilizes the principle that pressure of liquid within a tube tends to straighten the tube. A thin C-shaped steel tube is brought into connection with an artery. The pressure of the blood transmitted through the connections to the liquid with the C-tube will straighten it slightly. The proximal end of the tube being fixed, the distal end moves back and forth with each variation of pressure.

The mercury manometer gives a very exact measure of the amount of the pressure within the artery but the inertia of the mercury is too great to follow faithfully the minor variations of pressure: It shows the Traube-Hering curve, the respiratory wave and the systolic wave but it does not show the dicrotic wave. The spring manometer on the other hand shows the dicrotic wave as well as the others.

FIG. 105.



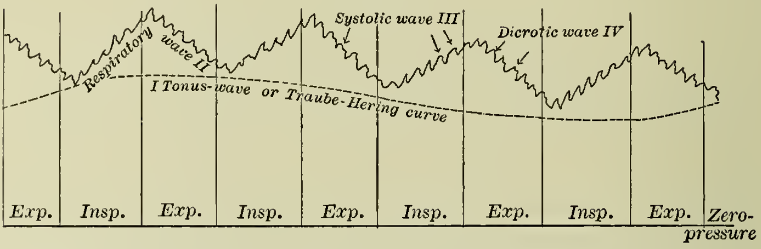
Showing the relation of arterial pressure to intra-ventricular pressure. Time relations: *a*, beginning of auricular systole; *b*, opening of semi-lunar valve; *c*, maximum of systolic pressure; *d*, closure of semi-lunar valves.

(*b*) RELATION OF ARTERIAL PRESSURE TO INTRA-VENTRICULAR PRESSURE.—As stated above, the arterial pressure is the transmitted, intra-ventricular pressure. The accompanying figure

(Fig. 105) shows that pressure within the aorta does not rise until the opening of the semilunar valves; that the crest of the systolic wave of aortic pressure coincides, near the heart, with the crest of the intra-ventricular (systolic) wave; that there is no "plateau" of pressure in the artery; that the closure of the semilunar valves marks the beginning of the fall in the ventricular wave and a superimposed (dicrotic) arterial wave; and that arterial pressure continues to fall until the semilunar valves open again.

(*c*) Variations of Arterial Pressure.—(*a*) *Cyclical variations* may be considered as: (I) Cycle of variation due to *heart contraction.* (See Fig. 106, Waves *III* and *IV.*) The rounded systolic wave, as shown by a mercurial manometer, or the systolic with its superimposed dicrotic wave, belongs to this class. (II) Cycle of variations due to the rhythmical action of the *respiratory* musculature. (See Fig. 106, Wave *II.*) Respiratory wave II is the result of the influence of the respiratory musculature. How is this result brought about? Note: 1st, that the pressure rises during inspiration; 2d, that it falls during expiration; 3d, that the maximum pressure occurs after the end of the inspiratory movement; and 4th, that the minimum pressure occurs after the end of expiration. The pressure rises during inspiration because there is greater negative pressure in the thorax, drawing more venous blood to the right auricle and leading either to a greater quantity of blood being ejected from the heart at each systole, or to an increase of the rate of the heart beats. (Sterling and others have observed the latter.) The pressure falls during expiration for reasons the converse of those just stated. The maximum pressure occurs after the end of inspiration and the minimum pressure after the end of expiration, because there is a lapse of about one second before the change wrought by respiratory movements can have its effect on the quantity of blood ejected from the *left ventricle.*

Fig. 106.

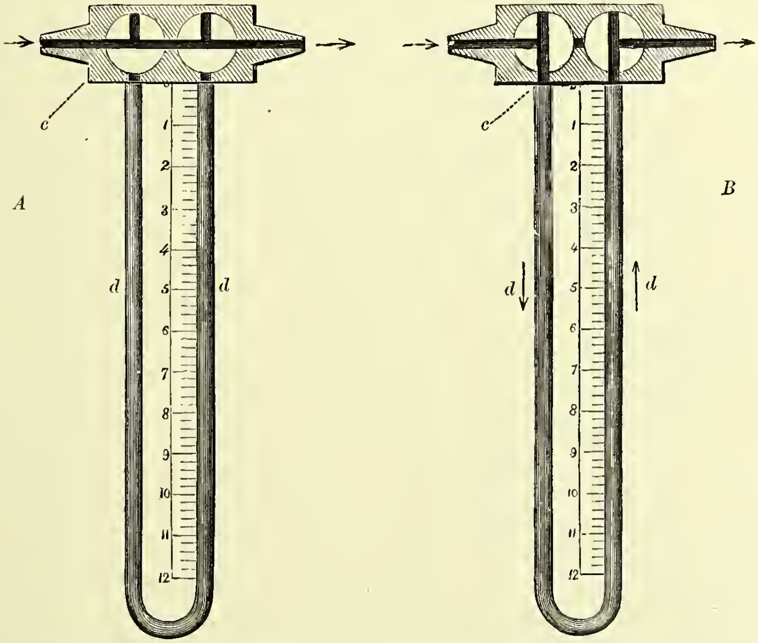


A typical tracing of arterial blood-pressure. *I,* Traube-Hering curve or tonus-wave is a wave of *I* order; *II,* respiratory wave, is a wave of *II* order, *i. e.,* superimposed upon *I. III,* systolic waves, are waves of *III* order, *i. e.,* superimposed upon *II. IV,* Dicrotic wave, is recorded by Fick's spring kymograph, is a wave of *IV* order.

(β) *Periodic variation,* due to changes in arterial tonus or to the degree of constriction under the influence of the vaso-motor nerves. (See Fig. 106, wave *I.*) These long waves are called Traube-Hering curves because first discovered and described by those whose names they bear.

3. **The Velocity of the Flow.**—(*a*) METHODS OF DETERMINING.—(*α*) *Volkmann's hæmodromometer,* shown in Figs. 107 and 108. As the cut indicates, this instrument consists of a U-shaped tube, about 25 cm. in length. The lumen of the tube is made continuous with the lumen of the artery by severing the latter and placing the proximal end over an entrance cannula and the distal end over an exit cannula. Two 3-way stopcocks control the entrance and exit. In the adjustment shown in the left-hand figure the blood passes directly through the instrument. When the cocks are turned as indicated in the right-hand figure the blood passes along the U-tube. In making an observation the tube was filled with water, which was driven into the artery when the tube filled. The time required for the stream to advance 25 cm. was taken to equal the velocity of flow in the artery of the same lumen. The results were far short of the actual velocity because of the resistance of the apparatus, and the contraction of the distal end artery due to the action of the water upon it.

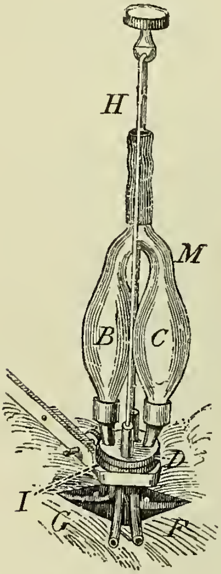
FIG. 107. FIG. 108.



Volkmann's hæmodromometer for measuring the rapidity of the arterial circulation.

(β) *Chauveau's dromograph* consisted of a brass tube to be inserted into the lumen of a severed artery. The blood flowing through the tube pressed against the lower end of a needle pivoted in the wall of the tube; deflecting it from its zero position by overcoming a resistance. The distal end of the needle indicated upon a dial the relative velocity of the stream within the tube.

FIG. 109.



Ludwig's stromuhr.

(γ) *Ludwig's stromuhr* is a modification of the principle used by Volkmann. The U-tube is replaced by a double chamber (Fig. 109) whose volume is known. Instead of stop-cocks, the chambers opening through plate D communicate with the cannulæ which open through plate I. After one of the chambers is filled the plate D is quickly rotated through 180°, with the aid of the milled head above H. This reverses the direction of the stream through the chambers. The proximal chamber (C) is filled with oil, the distal chamber (B) with normal saline solution, through the tube (H), which is thereupon clamped. The proximal cannula (F) is inserted into the proximal end of the cut artery. The plate D is turned just enough to shut off the continuity of the lumen. To make an observation, turn the plate D to 0°, taking the time to fifths of a second; the blood rushes through the proximal cannula up into chamber C; the oil floats upon the blood without mixing with it, and flows into chamber B, pushing the warmed saline solution into the distal portion of the artery. When the blood has reached the point at which the oil stood in the first adjustment the instrument is reversed, time noted, and the chamber B (now the oil-filled, proximal chamber) receives the blood from the proximal cannula (F), while the blood in chamber C is passed on into the artery.

With this instrument one determines in advance the *radius* (r) of the cannula, which is chosen for an artery of approximately equal radius; the *quantity* (q) which the chamber contains. During the experiment one observes the *time* (t) in seconds required to fill the chamber; n *number* of times. The following formula may be used: *Velocity* (v) equals a constant factor (K) multiplied by the number of times the chamber filled (n) and divided by the time (t) required to fill it n times, or $v = \frac{Kn}{t}$.[1]

---

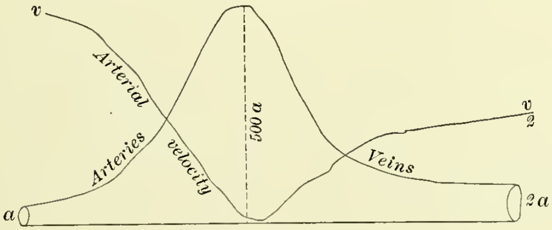
[1] The general formula given is derived thus:

(1) Discharge equals velocity times area of lumen: $D = va$.

(*b*) Variation of Velocity.—From the formula $v = \frac{D}{a}$, it is evident that the velocity will vary directly with the discharge and inversely as the area; $\left[v \text{ varies as } D;\ v \text{ varies as } \frac{1}{a}\right]$ in other words the velocity will be increased by anything which increases the discharge and by anything which decreases the sectional area of the vessels through which the blood flows.

(*a*) The *force and rate of the cardiac systole* cause a marked variation in the velocity of the flow. Experiments demonstrate that the discharge of a nozzle will be increased by increasing the height of water in reservoir above the nozzle (D varies as $\sqrt{h}$, see Physical Introduction) and further that the discharge will be increased under intermittent pressure when either the rate or force of the muscular contractions is increased, and much more if both rate and force be increased together. We may say then that *the velocity increases with rate of heart beat when all other variables remain constant and with force of heart beat other variables remaining constant.*

Fig. 110.



Relation of velocity to area.
Let arterial velocity $= v$
Venous velocity $= \frac{v}{2}$ or $\frac{1}{2} v$
Capillary velocity $= \frac{v}{500}$

When both rate and force are increased the velocity will be very much increased. When one of these factors increases while the other decreases the velocity may or may not be increased (v varies as rate × force).

(II) $\therefore v = \frac{D}{a}$.

(III) But $D = \frac{qn}{t}$ and $a = \pi r^2$.

(IV) $\therefore v = \frac{qn}{\pi r^2 t}$ or $\frac{q}{\pi r^2} \times \frac{n}{t}$; $\frac{q}{\pi r^2}$ is a constant quantity and may be represented by K, whose value may be calculated once for all for each instrument.

(V) $\therefore v = K\frac{n}{t}$ a general formula for the stromuhr.

(β) *The sectional area is also an important factor.* Anything which causes an increase in the sectional area will cause a decrease in the velocity; and conversely. "The velocity of the current in various sections of the vessels must be inversely as their sectional area." Volkmann determined the average velocity of the capillaries to be approximately $\frac{1}{500}$ as great as the velocity in the aorta. We may reason backwards and conclude that the combined sectional area of all the capillaries equals approximately 500 times the sectional area of the aorta at the base (see diagram, Fig. 110). The vaso-motor muscle-nerve system may induce variation of terminal sectional area and therefore influence velocity in periphery.

4. **The Pulse.**—Though this topic should logically come under consideration with (2) *Variations of Blood-pressure,* its importance clinically and the fact that a number of extra factors are involved in it justify a separate discussion.

The determination of blood-pressure with the Ludwig or Fick instrument is *immediate* or *direct* while the determination of the pressure by an examination of a superficially located artery is *mediate* or *indirect.* In the first case the character of the arterial walls or of the tissues overlying the artery cuts no figure while in the examination of the pulse these are important factors. Until comparatively recently no other means for the examination of the pulse has been used than palpation with the finger tips; even now this method is most important and the *tactus eruditus* reveals to the physician all important variations of the pulse.

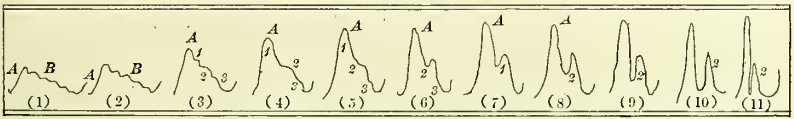
(*a*) INSTRUMENTS FOR RECORDING THE PULSATIONS of an artery are called *Sphygmographs.* There are several forms. The one in most common use by clinicians is the Dudgeon sphygmograph. An essential feature of this instrument is a system of compound levers which transmits the movement of the arterial wall from the foot or pad which rests upon the skin over the artery to a tracing point connected with the last lever. This system of levers multiplies the motion of the foot about fifty times. A second feature of the instrument is a recording apparatus consisting of a clock-work which turns a pair of small cylinders between which runs a slip of blackened paper. The tracing point rests upon this paper and records there the magnified movements of the foot or pad.

The *Sphygmograph* has the great advantage that it makes a record of the variation of pressure, and when properly used may reveal many facts about the general condition of the circulatory system. The disadvantages of this instrument are that slight variations in the location of the artery in different individuals lead to variations in the tracing; that accumulation of fat on the wrist may also "obscure" the artery and make the use of the sphygmograph difficult or make the results of no value; and, finally, faulty adjustments of the instrument lead to widely varying results with the same pulse. When the sphygmograph is used with all its disadvantages known and carefully weighed, or avoided, it may be a most valuable adjunct in physical diagnosis, especially for making a permanent record of a pulse for subsequent reference or comparison.

(*b*) THE PULSE-TRACING OR SPHYGMOGRAM.—It will be seen at once by reference to Fig. 111 that upstroke *A* and downstroke *B* represent the rise and fall in pressure due to ventricular systole and diastole. Obeying the general laws of liquids under intermittent pressure, the impulse, or *pulse*, is transmitted along the arteries as a wave or undulation of the arterial walls. The sudden upstroke *A* indicates the sudden influx of blood into the aorta during systole, while the gradual fall of the part *B* indicates the gradual fall of arterial pressure during diastole. The small waves, 1, 2 and 3, superimposed upon *B*, are called in order: 1. *Tidal wave*, or predicrotic; 2. *Dicrotic;* 3. *Postdicrotic.* The apex (*A*) is called the *Percussion wave* or *Systolic wave.* The dicrotic wave is due to the closure of the semilunar valves. The predicrotic and postdicrotic waves are due to the elastic tension of the arteries. Once set in motion the wall tends to continue to vibrate under the influence of a series of secondary waves.

These secondary waves fall into two classes. Fig. 111 gives a series of sphygmograms from normal individuals in widely varying states of blood-pressure, the highest pressure being shown in sphygmogram No. (1). From No. (1) to No. (11) the arterial blood-pressure is progressively lower, even merging into the pathological in Nos. (10) and (11), which were taken in the fever stage of acute "cold."

FIG. 111.



Sphygmograms from normal individuals.

The two classes of superimposed curves come out into prominence in this series: The Predicrotic and Postdicrotic waves as shown in Nos. (3), (4) and (5), which are typical, and average normal tracings, belong clearly to the class shown on the downstroke *B* of Nos. (1) and (2), where no dicrotic wave may be differentiated. There may be four, five or even six or seven of these wavelets on a high-pressure sphygmogram. They are called "*elasticity waves.*" With gradually decreasing pressure the less tense and very extensible arterial wall shows a decreasing tendency to transmit these waves until finally they are not discernible.

The dicrotic wave, however, is more and more pronounced with gradually decreasing pressure. Note wavelet 2 in tracings Nos. (3) to (11). In Nos. (3), (4) and (5) where we have both elasticity waves and the dicrotic on the tracing, the dicrotic is probably a resultant of two causes : (1st) the cause of the second elastic wave and (2d) the closure of the semilunar valves, because there would naturally be an elastic wave at 2 any way and beginning with tracing No. (3), some extra cause seems to be operating to emphasize or increase wavelet 2. Finally in tracing No. (6). The conditions necessary for the transmission of the elasticity waves have disappeared while the dicrotic continues to increase.

(*c*) Variations of the Pulse-rate are found to depend upon *age*, *height*, *muscular activity*, *state of the emotions*. Then besides a certain range of *individual variation* there is a wide range of *pathological variation*.

(*α*) Variation with *age:* At birth the rate is 130 to 140. By about the 18th year it gradually decreases to the average for adult life which is from 60 to 75 or not far from 70 per minute. This rate is maintained until the beginning of the senile period between the 50th and 60th year when there is a gradual increase to 80 or more per minute.

(*β*) Variation with *height:* Short individuals have a faster rate than tall ones ; a height of 140 to 150 cm. (4 ft. 8 to 5 ft.) corresponding to a rate of 74 per minute while 180 cm. (6 ft.) corresponds to 60 per minute.

(*γ*) There is a variation of the pulse rate with varying muscular activity, the rate being increased to a greater or less extent by exercise.

(*δ*) With emotional excitement the pulse may be greatly increased in rate.

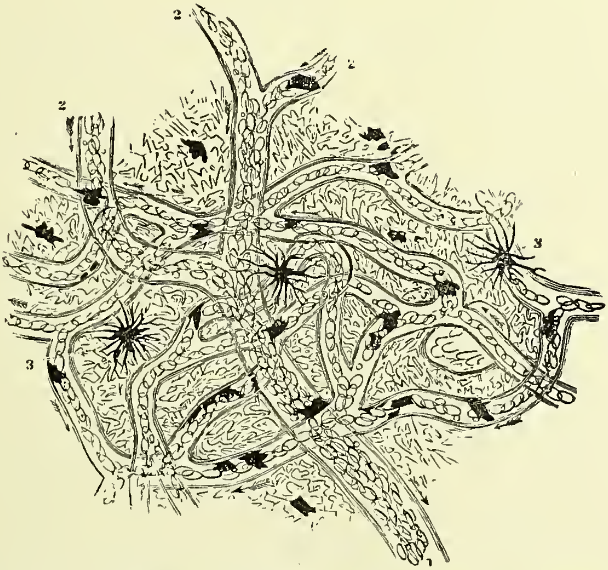
b. The Circulation in the Capillaries.

1. **Cause and Variations.**—The ultimate cause of the blood-pressure in the capillaries is, of course, the force of ventricular systole. Though the capillary pressure, and therefore capillary flow, is ultimately caused by systole, it is immediately varied by change in the lumen of the arterioles. If, for example, the local blood supply is increased, by a widening of the arterioles under the influence of the vaso-motor nerve-muscle apparatus, then the capillary pressure will be much increased. On the other hand, if the local blood supply be decreased through narrowing of the arterioles the capillary tension will be much decreased. In the first case the resistance offered by the arterioles is decreased, while in the second case it is increased. But the resistance offered by the arterioles is the variable factor of the peripheral resistance. The greater the arteriole resistance the less the capillary pressure

and conversely. Or it may be thus stated: The greater the sectional area of the arterioles the greater the capillary pressure, and conversely.

To sum up then: The capillary pressure varies, (I) directly as the energy of the heart's systole; and (II) directly as the sectional area of the arterioles. It may be further stated that the local capillary pressure, and consequently *local* plasma supply to the tissues varies directly as the *local* sectional arteriole area.

Fig. 112.



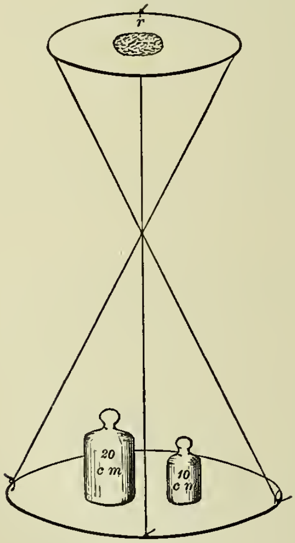
Capillary plexus in the portion of a web of a frog's foot, magnified 110 diameters. 1, trunk of vein; 2, 2, 2, its branches; 3, 3, pigment cells. (Carpenter.)

2. **Results.**—This relation between the condition of the arterioles and capillary pressure is a most important physiological fact. For a concrete case let us suppose that the blood, rich in foodstuffs from a recent meal, is on its way from the digestive organs to the general system; the individual resumes his work, which, let us suppose, is manual labor involving especially the muscles of the arms; the arterioles of the arms dilate; the local blood-supply is much increased, probably doubled; the veins and lymphatics are rapidly emptied by the working of the muscles; with the fall of tension in the arterioles has come an increase of capillary pressure, the increase is so great that the rich plasma is forced through the permeable capillary walls and bathes the muscle-cells. Under such conditions a certain amount of the waste products will enter the capillaries near their junction with the veins, where the pressure is low, but much will also leave the working

muscle by way of the lymph radicles and lymphatics, some will be retained and after a few hours the muscle will be fatigued, or will "feel tired"—a rest is in order. During rest the arterioles contract, capillary pressure falls and the accumulated products of destructive metabolism readily find their way into the capillaries, are carried to the organs of excretion and thrown out of the system.

3. **Method of Determining Capillary Pressure.**—Von Kries used a glass plate of known dimensions, to which was hung a scale-pan, the weight of the scale-pan and plate plus the weight necessary to exclude the blood from the capillaries equals the pressure for the area of the plate. If the area of the plate be 100 square millimeters; if the weight of the apparatus be 5 gms.; if the weight added to suppress capillary circulation be 22.2 gms., and if Pc be the capillary pressure per sq. mm., then $100\ Pc =$ 27200 milligrams; $Pc = 272$ mgs., Expressed in height of column of mercury: $Pc = \frac{272}{13.6} = 20$ millimeters of mercury. Several different methods have been used which involve the same principle.

Fig. 113.



Apparatus for determining the capillary pressure.

A slight modification of v. Kries's method (see Fig. 113) may be used. The plate which rests upon the finger has no raised plate of known area; it therefore becomes necessary to determine the area of the part from which capillary circulation is excluded. Suppose its diameter to be 8 mm.; weight of apparatus, 3.35 gms.; weight added to stop capillary circulation in area exposed, 20 gms.; total weight = 23.35 gms.

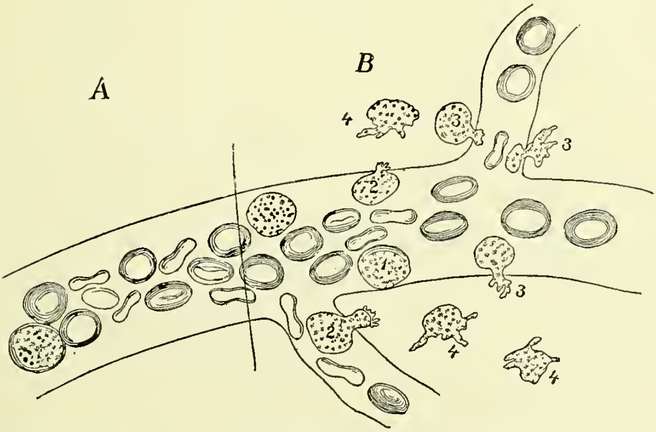
From the experiment above cited one may make the following general formula: $Pc = \frac{w}{ag}$ when $w =$ weight in milligrams; when $a =$ area in square mm.; when $g =$ sp. gr. of mercury. But $a = \pi r^2$, therefore the formula becomes:

$Pc = \frac{w}{\pi r^2 g} = \frac{1}{\pi g} \times \frac{w}{r^2}.$ But $\frac{1}{\pi g}$ is a constant quantity, w and r only being variable, so that we may give as a general formula for this apparatus: $Pc = K \frac{w}{r^2}.$ or *the capillary pressure equals a* *constant* (0.0234) *multiplied by the weight required to exclude the capillary circulation from an area and divided by the radius of the area squared.* The result thus obtained is in millimeters, and represents the height of a column of mercury which would balance the capillary pressure.

The various results of von Kries, Ray and others vary from 15 mm. Hg to 50 mm. Hg, according to the relation of the various factors involved in the capillary pressure at the time of determination. The position of the part has been found to be an important element. If the hand be held above the level of the shoulder, for example, the capillary pressure will be much decreased.

4. **Diapedesis.** (See Fig. 114.)—The term diapedesis is used to express *the passage of corpuscles through the capillary wall.* The passage of white corpuscles through the capillary wall is a normal process and is the result of an amœboid movement of the leucocyte; but the passage of red corpuscles is looked upon as an abnormal process by most physiologists. The process may be analyzed into several acts: (I) Adhesion to wall; (II) finding of opening by pseudopod; (III) the ameboid movements and flowing of protoplasm incident to traversing the wall; (IV) resumption of typical form and migration through tissues. The immense importance of this process was first emphasized by Conheim. In inflammation both red and white corpuscles (but the white are far more numerous) migrate in myriads into the tissues. Here the white corpuscles may be sacrificed for the good of the organism. Dead leucocytes are called *pus corpuscles.*

FIG. 114.



Diapedesis. 1, adhesion to wall; 2, finding opening by pseudopod; 3, traversing the wall; 4, resumption of active form; *A*, normal field; showing large capillary with corpuscles in center of blood stream; *B*, field of irritation, leucocytes leaving current and sticking to wall, causing a partial blocking of flow of red corpuscles.

c. The Circulation in the Veins.

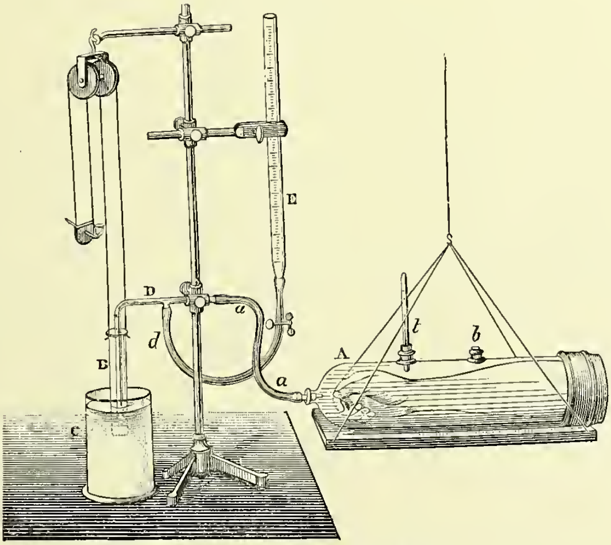
1. **Forces Involved in Venous Circulation.**—(α) Residuum of heart-pressure exerted through the capillaries. (β) Action of diaphragm and intercostals in causing negative intra-thoracic pressure during inspiration, actually lifting the column of blood in the ascending vena cava. (γ) Ventricular systole causing negative intra-thoracic pressure at end of systole and beginning of diastole, through the sudden decrease in volume of heart. (δ) Action of muscles pressing upon the veins. (ε) The force of gravitation, which materially assists in filling the ventricles and the left auricle, as well as in assisting the flow in the jugulars and descending or anterior vena cava, while it retards the flow in the veins below the heart. (ζ) Contraction of the mouths of the veins. (η) Under certain circumstances, positive intra-abdominal pressure, during inspiration and expiration (forced). (θ) Negative intra-thoracic pressure through pushing out of the anterior thoracic wall by the apex-beat of the heart.

Of these forces the first three are the efficient forces of venous circulation, the remaining forces are either so small in relation to the first three that they may be ignored or they act only under special conditions. The force of gravitation, though it assists the downward flow in all veins and retards the upward flow, may rather be recorded among the factors which modify venous circulation. Any action of the walls of the abdominal cavity (descent of diaphragm in inspiration or contraction of the lateral walls in expiration) will force toward the thoracic cavity any blood in the abdominal veins, but it will, to the same degree, keep out of the abdominal veins any blood in the legs.

2. **Causes and Variations of Venous Pressure.**—The forces involved in venous circulation, as enumerated above, are the causes of blood-pressure in the veins. These factors vary greatly in different parts of the venous system; *e. g.*, in the venules the principal factor is the residuum of heart-force. In the veins of the limbs one important factor is muscle-movement causing a flow toward the heart through a pressure exerted upon the walls of the veins; this increases the pressure within the veins and forces the blood to move in the direction of least resistance.

The distal flow is blocked by the valves of the veins and the flow toward the heart is thus increased. In the large venous trunks near the thorax the negative intra-thoracic pressure—caused by inspiration, by cardiac systole and by the apex beat—is the principal factor of venous circulation, operating not by causing higher pressure at the periphery, but by causing lower pressure at the center. The quickening of venous circulation through muscle-movements, whether these movements be passive or active, is the basis of the theory of massage. All the varied phases of massage treatment have developed from this point, and all have the effect of quickening venous and lymphatic circulation primarily and of recuperating and rejuvenating the tissues secondarily. Active muscular exercise not only quickens venous and lymphatic circulation directly in the manner described, but also indirectly through causing an increase in the frequency and strength of ventricular systole and furnishing a larger residuum of cardiac force for venous circulation.

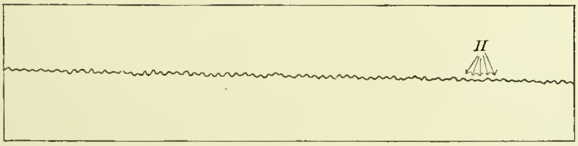
Fig. 115.



Plethysmograph of Mosso. (Marey.)

3. **The Plethysmograph.**—This instrument comprises a metallic or glass case which is made to enclose an arm or leg, the open end of the case being closed with guttapercha (see Fig. 115). A small tube from the plethysmograph connects with a pressure apparatus, and another with a recording tambour. Any changes

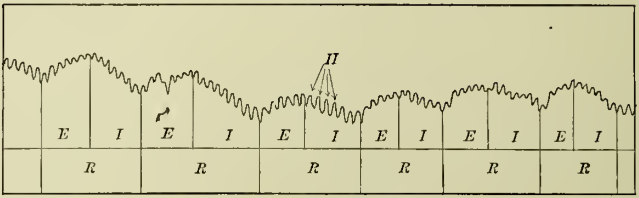
Fig. 116.



Plethysmogram. Respiration was suspended. The small waves *H* are due to the influence of the heart alone.

in the volume are accurately recorded by the tracing lever upon a kymograph drum. The accompanying plethysmograms taken by the author during a class demonstration show the general influence of the circulation upon the volume of the arm.

FIG. 117.

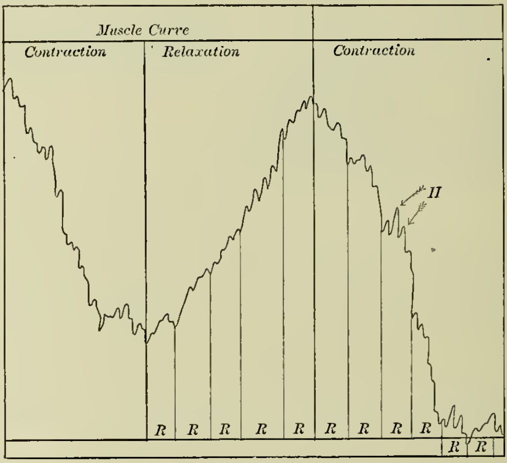


Plethysmogram. The influence of respiration is added to that of the heart. *R*, indicates respiratory wave; *E*, exspiratory portion; *I*, inspiratory portion.

These tracings justify the following conclusions:

Fig. 116. The volume of the arm (or other portion of the body) is affected by the cardiac contractions.

FIG. 118.



Plethysmogram. The influence of muscular contraction is added to that of respiration and heart contractions. The arm is emptied and the curve drops during contraction. The respiratory waves are well marked in portions of the tracings.

Fig. 117. The volume of the arm is influenced by the respiratory movements, being increased during expiration and decreased during inspiration. The reason for the decrease during inspiration is that the increased negative intra-thoracic pressure empties the veins of the arm.

Fig. 118. The volume of the arm is influenced by muscular movements, being increased during relaxation and decreased during contraction. The reason for the decrease during muscular contraction is that the pressure of the contracted muscles upon the veins and lymphatics empties them toward the heart. This is a demonstration of the validity of the point given above [*C*, (1), (*d*)], where muscular contraction was given as one of the forces which cause venous blood flow.

3. THE CIRCULATION OF THE LYMPH.

a. In the Lymph Radicals.

1. **Causes and Variation.**—After the plasma has oozed through the capillary wall and become lymph, it receives pressure from three sources : (I) The capillary pressure which caused it to filter through the capillary wall is not all expended in that process ; or, expressed differently, as long as more plasma is passing into the tissues, the plasma or lymph already there is forced on through the minute lymph radicals. (II) Endosmosis is the principal physical factor of lymph circulation in the lymph radicals of the intestinal mucous membrane. (III) The physiological factor *selection* plays a still more important rôle, but it cannot be measured. Variation of any of these factors—the first through variation of capillary pressure, or the second and third through the conditions in the alimentary canal—will cause a variation of pressure, and, as a consequence, a variation of the flow in the lymph radicals.

b. In the Lymphatics.

1. **Causes and Variation.**—(I) *Residuum of the pressure* in the lymph radicals is a strong factor. (II) The most important factor of lymph circulation in the limbs is *muscular activity.* As is the case with the venous circulation, so here the efficiency of muscular activity depends upon the presence of valves within the vessels. The numerous lymphatic glands in the course of the lymphatics—especially in the axilla and groin—act somewhat like valves in staying the reflux of the column of lymph after it has once passed. (III) In all those lymphatics near the thorax the negative pressure of that cavity during inspiration acts as a strong motive factor. Variation of muscular activity is the most important variable factor in the lymphatic circulation.

E. THE CONTROL OF THE ORGANS OF CIRCULATION.

1. THE INNERVATION OF THE CIRCULATORY SYSTEM.

When we remember that the general flow of blood, in response to arterial pressure, is affected directly by the activity of the heart and reciprocally by the sectional area of the arterioles and capillaries it is clear that the problem of determining the exact status of the circulation can only be solved by knowing the value of both variable factors, which solution is not facilitated by the fact that both the heart-activity and the sectional area of the arterioles are variously affected by different local and general stimuli. These different stimuli affect the circulatory organs usually through the medium of the nervous system though certain stimuli may act directly upon the muscle tissue of the heart or arteries.

FIG. 119.

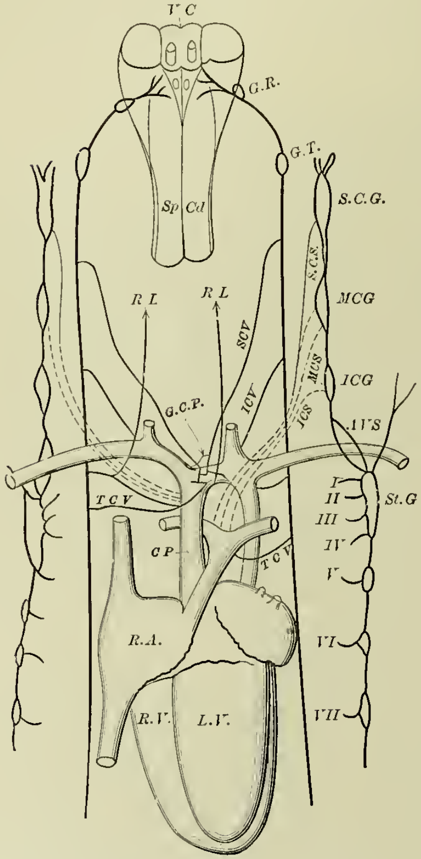


Diagram of the nerve supply of the heart. Continuous lines show vagus origin of cardiac plexus; dotted lines show sympathetic origin of that plexus. *VC*, vagus center in floor of 4th vent.; *SCS*, Cardiac branch of the sup. cerv. symp.; *MCS*, cardiac branch of the mid. cer. symp.; *I–VII*, rami communicantes from spinal cord to ggl. of symp. syst.; *ICS*, inf. cerv. symp. cd. br.; *CP*, Cardiac plexus. Shown only in part, in the Fig. *Ct*, *Cd*, *Pl*, Beside arch of aorta. (2), ant. cd. pl. under arch of aorta. (3), coronary plexuses are really div. of the gen. cardiac plexus; *TCV*, thoracic card. br. of vagus; *GR*, ganglion of vagus root; *GT*, ganglion of vagus trunk; *SCV*, sup. cardiac br. vagus; *ICV*, inf. cardiac br. vagus; *RL*, recurrent lary., giving branch to cardiac plexus; *GCP*, great card. pl. of vagus and sympathetic fibers; *SCG*, superior cervical ggl. symp., *MCG*, med. cervical ggl. symp.; *ICG*, inf. cervical ggl. symp.; *StC*, stellate gang. sympathetic; *A Vs*, Annulus of Vieussens around subclavial artery.

a. The Innervation of the Heart.

1. The Heart as Influenced from Within.—The heart of an amphibian or reptile has a ganglion in the venous sinus—Remak's—one in the interauricular wall—the ganglion of Ludwig or v. Bezold—and a pair of ganglia in auriculo-ventricular septum—Bidder's. The heart of the mammal differs from this only in having a group of several ganglia where the frog or turtle has one; but the three groups of ganglia in the mammalian heart are looked upon as anatomically homologous to the correspondingly located single ganglia of the amphibian heart, and as physiologically equivalent to them. General laws based upon experiments with cold-blooded animals hold good for mammals. The heart of a frog continues to beat some time after removal and is especially adapted for certain experiments. *Stannius's* experiment consists in first cutting off from the auricles and ventricles, through ligature or incision, the influence of Remak's ganglion, the auricles and ventricles become quiet: Second, dividing by ligature or incision, auricles and ventricle at their junction—the ventricle begins to beat, the auricles remain quiet. The experiment was formerly interpreted thus: The heart muscle acts under the influence of three ganglia—or groups of ganglia—Remak's and Bidder's ganglia afford positive stimulation, while the Ludwig ganglion or group of ganglia retard or inhibit the heart action. The influence through Remak's and Bidder's ganglia exceed the influence of the Ludwig ganglion; therefore when all are intact, the heart beats. When the influence of Remak's ganglion is removed the influence of the Bidder's ganglia is not sufficient to overcome the inhibition of the Ludwig ganglion; therefore, the auricles and ventricles stand still. When the inhibitory influence of the Ludwig ganglion is removed the ventricle starts into activity. This ingenious and plausible theory has been shaken by the investigations of Gaskell and others. They have found that when properly stimulated and nourished, small pieces of the ventricle, which are wholly free from ganglia, will continue to beat rhythmically for a considerable period; further, that special stimuli are transmitted through muscle tissue. It appears from this that THE RHYTHMICAL BEATING OF THE HEART HAS ITS IMMEDIATE CAUSE IN THE PROTOPLASM OF THE MUSCLE CELLS. The *beat* may be *varied* in *rate* and *force* by *stimuli affecting* the *cells from without*. Whether any part of this extracellular stimulus *originates* in the cardiac ganglia is still an open question. These ganglia *may* act merely like storage centers or distributing centers for the central nervous system.

From the Stannius experiment it seems that the cardiac ganglia may affect the rate and force of the heart-beat; but we must not forget that in this experiment a profound departure from any possible normal condition is made and we must not impose too much confidence in the inductions derived from the effects. From the connections of the cardiac ganglia with the cardiac plexus of nerves we should expect their function to be for the most part *mediate*.

2. **The Regulation of the Heart by the Central Nervous System.**—If the cardiac plexus of a dog be followed upward from the mouth of the anterior vena cava it will be found to represent two symmetrically located sources, one to the right and one to the left. If we follow the left we will find the three or more nerve trunks converging toward the inferior cervical sympathetic gang-

lion. Here there are connections anteriorly along the vago-sympathetic trunk toward the brain and laterally via the Annulus of Vieussens, to the first thoracic ganglion of the sympathetic. Whether these connections represent *afferent* or *efferent* nerves is impossible to determine by other means than by physiological experimentation. Suppose the vago-sympathetic trunk to be divided high up in the neck and the distal end stimulated with an induction current, the result will be a slowing or stopping of the heart-beat ; if the stimulation be made lower down and at different points the result will be the same until the inferior cervical ganglion is reached, when the results will be variable and ambiguous. If the Annulus of Vieussens be divided and the distal ends stimulated there will be either acceleration of the *rate* of beat or augmentation of the *strength* of beat of the heart. If the Rami Communicantes II or III be divided and stimulated distally there will be acceleration or augmentation of heart activity. From these experiments we may conclude that the vago-sympathetic trunk (in man the vagus) contains fibers whose stimulation causes slowing or INHIBITION of the heart-beat, while the sympathetic contains fibers whose stimulation has the reverse effect, *i. e.*, that of ACCELERATION or AUGMENTATION. Through further experimentation the *inhibitory* fibers may be traced along the vagus through the jugular foramen, along the trunk of the spinal accessory to its origin in the floor of the fourth ventricle in the posterior part of the medulla oblongata. In a similar way the accelerator fibers may be traced through the Rami Communicantes, along the anterior nerve roots into the spinal cord, and up to the medulla oblongata where its exact origin has not been determined. In man the main cardiac branch of the sympathetic is called N. Accelerans cordis, and is not ensheathed with the vagus in any part of its course.

We have now found that the inherent property of the heart muscle to produce an uninterrupted series of alternating contractions and relaxations is governed by the central nervous system in a way analogous to the way in which a horse is governed by the driver ; the inhibitory vagus-fibers checking the speed of the heart-beat and the acceleratory fibers of the sympathetic stimulating the heart to greater speed, or greater force, as the case requires. But what causes the central nervous system to send these messages of inhibition or augmentation to the heart? Here we must recall the general principle that, *all messages sent out from the central nervous system*—all efferent nerve impulses—*are in response*, (I) *to afferent nerve impulses*, brought to the central nervous system through nerves which carry impulses only from the periphera to the center—the sensory nerves ; (II) to direct stimulation of the center. As an example of (I) the sudden withdrawal of the hand from a needle point is accomplished through contraction of muscles in the arm in response to an efferent motor message from the center which in turn is stimulated by the afferent message of pain from the skin, reaching the center through a sensory nerve. If we look for the afferent nerves—sensory nerves—which carry messages to the center from the heart or some part of the periphery we shall find them represented by only the general sensory nerves, either spinal or sympathetic, and these affect the heart-beat only indirectly, after a too complex inter-central interchange to be accepted as a simple reflex. We must look for another way in which the center may be affected. (II) The *center* may, however, be *directly stimulated.* Physiological examples of the direct stimulation of a center are not numerous and are confined for the most part to the circulatory and respiratory centers. This direct stimulation of respiratory and circulatory centers is made possible by the fact that the activity of these organs is directed toward the supply of the system with blood sufficient in quantity and proper in quality. The nerve centers in the medulla being a part of the system so supplied, are at once affected by variations in blood-pressure or in the quantity of CO_2 and of O brought by the blood-supply.

(*a*) STIMULATION OF THE CARDIO-INHIBITORY CENTER, *followed by slowing of the heart-beat.* (*α*) *Direct.*—(I) Sudden anæmia of the medulla oblongata, as would be produced experimentally by ligation of the carotids and vertebral arteries. (II) Sudden venous hyperæmia in the medulla oblongata, as would be produced experimentally by ligation of the jugular veins. (III) By increase of the CO_2, as would occur in suspended respiration, thus any interference with a proper oxygenation of placental blood during pregnancy or parturition will cause a slowing of the fœtal heart-beats. (IV) Increased blood-pressure in the cerebral arteries.

(*β*) *Indirect.*—Strong stimulation of any sensory nerve, *e. g.*, tapping the exposed intestines of a frog with a scalpel handle will cause inhibition of the heart.

(*b*) STIMULATION OF CARDIO-ACCELERATOR, or cardio-augmentor centers, followed either by acceleration of rate, or augmentation of force, or both.

Stimulation may be direct or indirect, but uncertainty about the location of the center confines our knowledge to that gained by a stimulation of accelerator fibers which always, of course, causes acceleration or augmentation of heart activity with associated rise in blood-pressure. Indirect stimulation of the cardio-accelerator center is illustrated in the sipping of cold water, which has a strong accelerating effect upon the heart, probably through stimulation of the cardio-accelerator center, through afferent fibers of the sympathetic nervous system.

3. **The Mechanical Stimulation of the Heart.**—(*α*) Through increased flow of blood to the heart due to negative intra-thoracic pressure. This increase of blood in the heart cavities seems to stimulate it directly without the intervention of the nerve-apparatus.

(*β*) Through increased resistance in the aorta; due in turn to increased peripheral resistance.

b. The Innervation of the Arteries.

Though the arterioles and small arteries may change their caliber through such local influences as changes in temperature, their variations in caliber are, for the most part, due to the influence of nerves upon the circular muscle-fibers. The nerves which control the arterial supply of the muscles are called VASO-MOTOR NERVES. Experiment has proven that there are two kinds of nerves supplying the arteries, as there are two kinds of nerves supplying the heart: (I) there are fibers which augment the tonicity of the vessels by causing contraction. These nerves are called VASO-CONSTRICTOR NERVES; (II) there are fibers which inhibit the stimulus given to the muscles by the vaso-constrictor nerves, these are called VASO-DILATOR nerves. To get a clear idea of the action of vaso-constrictor and vaso-dilator nerves it is necessary to take a concrete case. The *submaxillary salivary gland* is supplied by two nerves: (I) a branch of the sympathetic which accompanies the artery; (II) the chorda tympani nerve. Both of these nerves supply fibers to the arterioles of the gland. Under the influence of the sympathetic the arterioles are kept usually in a state of moderate contraction called "tonus." This condition of tonus, which is the usual condition of all the small arteries and arterioles of the body, is maintained by rapidly repeated moderate stimuli passing from the vaso-constrictor center in the medulla oblongata out to the arteries in all parts of the body. If these stimuli are increased or decreased the tonus becomes higher or lower accordingly, *i. e.*, the vessels are constricted by the contracting circular muscles, or they are dilated by the blood-pressure after relaxation of the circular muscles. To return to our example—the arterioles of the submaxillary salivary gland are governed by the general condition of the vaso-constrictor apparatus; and, according as the general tonus is high or low, the local blood supply will be under higher or lower pressure, but not necessarily modified in quantity. If an especially free local blood supply be necessary—as is the case when the gland is actively secreting—some local inhibitory influence must be brought to bear upon the vaso-constrictor nerves to suspend their action and to allow the arterioles to dilate widely under the influence of the blood-pressure. This local inhibitory influence is furnished by the chorda tympani nerve, which is called a vaso-dilator and has upon the muscular tissue of the arteries an influence analogous to that which the vagus has upon the muscle tissue of the heart. From this it would seem that the primary function of the vaso-constrictor nerves is to govern general blood-pressure through general changes in the tonus of the small arteries and arterioles, thus increasing or decreasing terminal resistance.

The above example further indicates that the primary function of the vaso-dilator nerves is to control local blood supply through suspending the action of vaso-constrictors, thus allowing the blood vessels to dilate. This is in general the relation of the two systems of vaso-motor nerves.

1. **The Vaso-constrictor System: Tonus of Blood Vessels.**— The vaso-constrictor center was located by Ludwig and his pupils in the floor of the fourth ventricle—in the medulla oblongata. That this is a general center is proven by this experiment. Stimulation causes general contraction of all the arteries; while paralysis of the center, as by over-stimulation, causes general dilatation. From this center nerve fibers pass down the lateral tracts of the spinal cord, from which they emerge through the anterior nerve roots and pass into the sympathetic system through the rami communicantes. From the sympathetic system they supply all arteries of the body cavity and some of the arteries of neck and mouth as branches of that system; while the arteries of the skeletal muscles and skin are supplied by branches which have left the sympathetic system and are distributed along with branches of the spinal or cranial nerves. Besides this general center in the medulla there are local centers in the gray matter of the spinal cord; further, some of the ganglia of the sympathetic system may act as local centers. The action of the local centers may cause a local change in arterial tonus.

(*a*) DIRECT STIMULATION OF THE VASO-CONSTRICTOR CENTER.—(I) An excess of CO_2 in the blood supplying the center acts as a stimulus and causes a constriction of the arteries in general. (II) Sudden anæmia of the medulla as the effect of a severe hemorrhage or of ligation of the arteries bringing the local supply. (III) Venous hyperæmia as the effect of the ligation of the jugulars. It is probably the excess of CO_2 which is active in this case. (IV) Poisons, *e. g.*, strychnia, nicotine, etc.

(*b*) REFLEX STIMULATION.—(I) Through "*pressor*" afferent nerve fibers whose stimulation may cause a reflex constriction of the arteries generally. (II) Through "*depressor*" afferent nerve fibers. These are not widely disseminated; most of them are located in the depressor nerve (superior cardiac in man), which passes upward from the ventricular walls, through the vagus to the vaso-motor center. The ventricular termini of this nerve are stimulated by an excessively high arterial pressure. The return passage is not sent to the heart, but to the vaso-constrictors of the abdominal cavity, and takes the form of an inhibition, in consequence of which the arteries of the abdomen relax, the blood-pressure falls and the heart is relieved of its excessive work.

2. **The Vaso-Dilator System.**—That there is a system of nerves emanating from a special center, whose function is to suspend or inhibit locally the general action of the vaso-constrictor system is abundantly proven by such physiological experiments as that upon the submaxillary gland. It has been further proven that the center is in the medulla—or at least above the spinal cord—but its exact location has not been determined. The distribution of the vaso-dilator fibers is in a general way parallel to that of the vaso-constrictor fibers; they may supply a particular locality in the same trunk with vaso-constrictor, motor and sensory fibers, or they may form a separate nerve, as is the case in the chorda tympani. All vaso-motor fibers are efferent; the afferent members of the reflex circuit is represented in part by the blood supply of the center in the case of the vaso-constrictor center. This condition is possible in that case because the influence of the vaso-constrictor system is for the most part general; but the local action of the vaso-dilator system makes direct stimulation of the vaso-dilator center practically impossible. As no afferent vaso-dilator fibers have been found, it is probable that the afferent member of the circuit is represented by the sensory nerve coming from any given locality.

2. ADAPTATIVE COÖRDINATION OF THE ACTIVITIES OF THE CIRCULATORY ORGANS.

In our study of *motion* in general physiology we found that a successful adaptative motion must be coördinated in time or in space and time and controlled in force. In the same way the activities of the circulatory organs, depending as they do, upon muscle contractions, must be *perfectly coördinated* in *time* and controlled in force. This is accomplished, as we have seen, through the central nervous system; its coördinating messages are sent to the heart and arteries through augmentor and inhibitory cardiac and vaso-motor fibers. Through the agency of this most complicated nerve apparatus the following general adaptative adjustments are accomplished:

I. Regulation of temperature.
II. Regulation of secretion and excretion.
III. Regulation of supply of food and oxygen to working organs.
IV. Regulation of general blood-pressure.
V. Regulation of local blood flow: To secreting glands; to working organs; in blushing; in pallor, etc. Most of these will be discussed under different headings.

CHAPTER IV.

RESPIRATION. INTRODUCTION.

RESPIRATION DEFINED AND CLASSIFIED.

A. COMPARATIVE PHYSIOLOGY OF RESPIRATION.

1. RESPIRATION IN INDIVIDUALS OF A LOWER ORDER.
2. RESPIRATION IN INDIVIDUALS OF A HIGHER ORDER.
   (1) Cutaneous Respiration.
   (2) Respiration by Gills.
   (3) Respiration by Lungs.

B. ANATOMICAL INTRODUCTION.

THE HISTOLOGY OF THE RESPIRATORY ORGANS.

C. PHYSICAL INTRODUCTION.

THE SOLUTION OF GASES IN LIQUIDS.

RESPIRATION.

INTRODUCTION.

RESPIRATION DEFINED AND CLASSIFIED.

From our studies in general physiology we know that that peculiar form of *energy* which we call *life* exists only in association with living cells or with living organisms, that it is liberated only through a katabolism or destructive metabolism of living cell protoplasm and that this katabolism is possible in the presence of oxygen. The frequent use of such expressions as "*The spark of life*," "*The flame of life*," etc., indicates the analogy between the liberation of life energy and the liberation of the heat and light-energy of fuel. It was once thought that these two processes were quite alike—each being a *combustion* or direct oxidation. The oxygen of the atmosphere unites directly with the carbon and hydrogen of the candle, of wood, of coal, or of illuminating gas to form CO_2 and H_2O—the process being attended with the liberation of energy ; now the oxygen of the atmosphere forms combinations in the tissues and the combinations finally result in the formation of CO_2, H_2O and CON_2H_4—the process being attended with the liberation of life energy. These two processes which seem so much alike are essentially different in a very important point. In the combustion of the hydrocarbons of the candle the affinity of oxygen for the carbon and hydrogen is so great that, if once started the combustion proceeds by the invasion of the molecules by the oxygen, which breaks the bond between carbon and hydrogen and joins with each.

In the katabolism of the living protoplasm of the cell, the exceedingly complex protoplasmic molecule separates into two, perhaps more, simpler molecules; these simple molecules, which probably represent proteids, may again separate into still simpler ones. Each change from a complex to a more simple compound leads (I) to a liberation of energy, which may manifest itself in any of the activities of life, and (II) to a combination of simpler molecules with oxygen furnished by the cell sap or cell plasma. In the latter case, then, the oxygen steps in to complete a molecule already nascent, while in the former case it is the *cause* of dissolution. To sum up the comparison: *Oxygen is the cause of combustion but the complement of katabolism.* This general process of supplying the cells of a living organism with the requisite oxygen is called *Respiration.*

1. **Definition.**—Respiration is a general term which includes all of those activities involved in the furnishing of oxygen to the tissues of a living organism.

2. **Classification.**—The essential act of respiration is the taking up of oxygen by the living cell from the tissue plasma. In the large animals a more or less complex series of preliminary acts are necessary in order to furnish the tissue plasma with oxygen, and of this series of acts the interchange of gases between the blood and the medium surrounding the animal is the most prominent. This has led to the following classification: (I) Internal respiration or cell respiration. (II) External respiration or somatic respiration.

A. COMPARATIVE PHYSIOLOGY OF RESPIRATION.

1. RESPIRATION BY INDIVIDUALS OF THE I, II, AND III ORDER.

It has just been stated that the oxygen required in the cell at the moment of katabolism is furnished by the cell sap or cell plasma in which it is held in simple solution. If the cell is an independent organism, *e. g.*, an amœba, the oxygen of the cell plasma is immediately replenished from the water which surrounds the amœba. This is respiration in its simplest form. If the organism be an individual of the II or III order the process is essentially the same.

2. RESPIRATION IN INDIVIDUALS OF THE IV ORDER.

1. **Cutaneous Respiration.**—The common earthworm or angleworm has well developed digestive, circulatory, nervous, repro-

ductive and motor systems, but has no definite respiratory system. It has been found that the rich cutaneous capillary plexuses furnish to the blood an ample supply of oxygen which finds its way easily through the delicate cuticle, attracted by the low oxygen-pressure in the cutaneous capillaries. In the amphibia the moist skin facilitates the diffusion of oxygen and in this class of vertebrates cutaneous respiration is important though always secondary to respiration by gills or lungs. A frog can live some time after the lungs have been removed.

2. **Respiration by Gills.**—Many invertebrates, *e. g.*, mollusca and aquatic arthropoda and all lower vertebrates, including tunicates, Enteropneusta, Amphioxus and all fishes breathe by means of gills. A gill is an organ presenting numerous filamentous branches whose delicate covering membrane affords slight resistance to the diffusion of oxygen into the blood from the water with which the gill is bathed.

3. **Respiration by Lungs.**—Most amphibians and all reptiles, birds and mammals breathe atmospheric air into sac-like organs called lungs. The environment and habits of these animals necessitate the protection of the lungs within the body cavity. Here the blood in the capillaries is distributed over the surface of the minute air-cells and the air, which has been warmed and freed from dust in its passage through the air channels, exchanges its oxygen easily through the thin, moist membrane of the air sac for the excess of CO_2 in the blood.

B. ANATOMICAL INTRODUCTION.

The *skeletal features* particularly important in considering the physiology of respiration are summarized below under physiology of respiration because it contains matter not introduced into the anatomies, and intimately and indissolubly associated with the physiology of the mechanics of respiration.

For the same reasons the *muscles of respiration* are enumerated and classified under mechanics of respiration.

The following additional facts of gross anatomy should be noted :

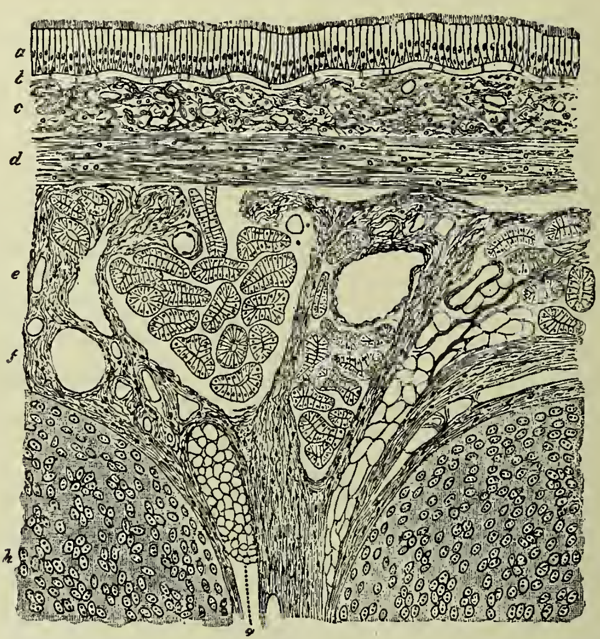
(*a*) THE NASAL RESPIRATORY PASSAGES are tortuous, irregular in lumen, lined with a mucous membrane always well moistened with mucus, and provided, near the external opening, with numerous rather stiff hairs. The effect of this structure is to warm and free of dust the inspired air.

(*b*) THE RESPIRATORY TRACT CROSSES the alimentary tract in the pharynx, a cavity common to both tracts. The respiratory passage is protected during the act of swallowing : (I) posteriorly by the epiglottis and the adduction of the vocal cords (for details see deglutition) ; (II) anteriorly by the elevation of the soft palate, and the elevation of the uvula. (See deglutition.)

(*c*) The Trachea and Bronchi are Strengthened and held open by heavy rings of cartilage. Thus protected the air passages remain open even when subjected to considerable pressure.

(*d*) The Trachea and Bronchi are Lined with a ciliated columnar epithelium, which is kept moistened with mucus secreted by the mucous glands of the submucosa as well as by goblet cells. The ciliary motion carries all secretions as well as particles of dust which pass the barriers in the nasal passages, upward toward the larynx from the deeper passages of the lungs. (See Figs. 120 and 121.)

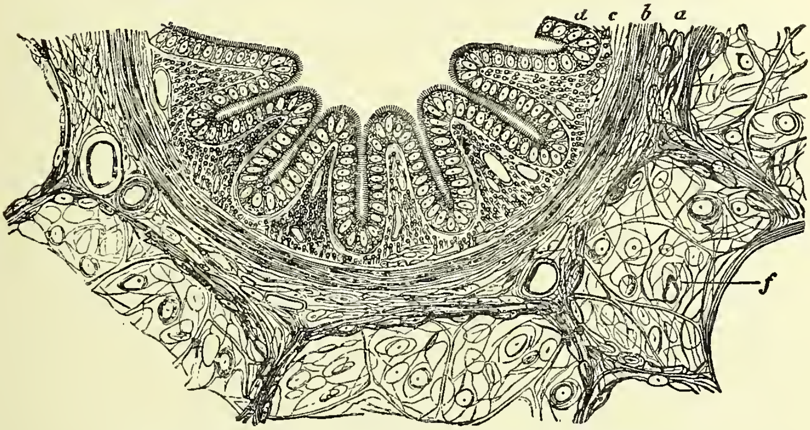
Fig. 120.



Longitudinal section of the human trachea, including portions of two cartilaginous rings. (Klein.) (Moderately magnified.) *a*, ciliated epithelium; *b*, basement-membrane; *e*, superficial part of the mucous membrane, containing the sections of numerous capillary blood vessels and much lymphoid tissue; *d*, deeper part of the mucous membrane, consisting mainly of elastic fibers; *c*, submucous areolar tissue, containing the larger blood vessels, small mucous glands (their ducts and alveoli are seen in section), fat, etc.; *f*, fibrous tissue investing and uniting the cartilages; *g*, a small mass of adipose tissue in the fibrous layer; *h*, cartilage. (Schaefer.)

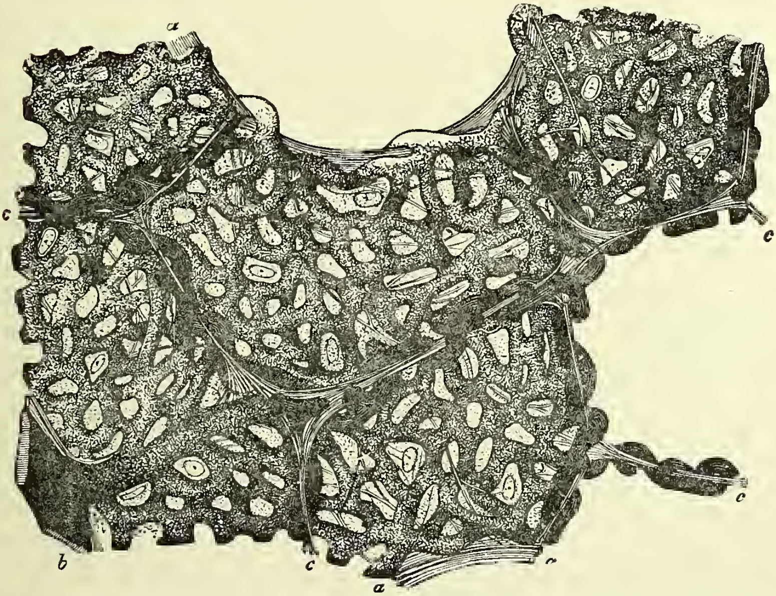
(*e*) The Trachea Branches into two large bronchi, of which the left subdivides into two and the right into three subdivisions. The five branches subdivide dichotomously, until every lobule of the lung is supplied with a fine terminal bronchus which ends in delicate saccate air spaces or alveoli. "The part of the pulmonary parenchyma in communication with a single terminal bronchiole forms a pyramidal mass, whose apex corresponds to the terminal bronchus and whose base, when reaching the free surface of the

Fig. 121.



Section of a small bronchial tube from a pig's lung. (Schaefer.)

Fig. 122.



Section of injected lung, including several contiguous alveoli. (F. E. Schultze.) (Highly magnified.) *a*, *a*, free edges of alveoli; *c*, *c*, partitions between neighboring alveoli, seen in section; *b*, small arterial branch giving off capillaries to the alveoli. The looping of the vessels to either side of the partitions is well exhibited. Between the capillaries is seen the homogeneous alveolar wall with nuclei of connective-tissue corpuscles and elastic fibers. (Schaefer.)

lung, appears as one of the polygonal areas marking the exterior of the lung." (Piersol.)

This pyramidal mass is called a *lobule.* Within the lobule the *terminal bronchus subdivides* into *two or three alveolar ducts,* beset with air-sacs, and the *alveolar ducts,* without subdivision, *open into or widen out into, "blind" irregular, or pyramidal* spaces the *infundibula.* The infundibulum is beset on all sides with air-sacs which open into the infundibulum but do not communicate with each other.

(*f*) The Impure Blood, brought from the right heart by *the pulmonary artery,* is distributed to the lung tissue through branches which follow the subdivisions of the bronchi finally reaching the lobule as an arteriole which subdivides into a network of fine capillaries lying in the walls of the alveoli or air-sacs. The venous blood is thus brought into intimate relation with the atmospheric air which enters the alveoli. Fig. 122 shows the capillary network which surrounds the alveoli.

D. PHYSICAL INTRODUCTION.

THE SOLUTION OF GASES IN LIQUIDS.

If one were to place a liter of hydrant water under the receiver of an air pump, he would find that the water subjected to a vacuum would give off gas vigorously; the quantity depending upon the conditions which had existed before the experiment. An analysis of this gas would show it to be nitrogen, oxygen, and carbon dioxide, or the same gases to which the water had been exposed in its contact with the air. If we expose H_2O to an atmosphere of HCl gas it will rapidly absorb large quantities, forming the common hydrochloric acid. So it becomes evident that water may hold considerable quantities of gases in solution. Just how much gas any liquid will absorb depends upon the nature of the gas and the nature of the liquid; but the amount of any particular gas which a particular liquid will absorb varies with the pressure of the gas in the atmosphere to which the liquid is subjected. For example, if the amount of oxygen in the air were doubled, water would absorb twice as much; but if it were reduced to one-half or one-third of its present proportion, water would absorb proportionately less. Any change in the proportion in the air is quickly responded to by a readjustment of the proportion in the water through simple diffusion, to again reach an equilibrium.

The following laws have been formulated by McGregor Robertson (Physiological Physics, p. 291):

(*a*) The Gases Most Readily Liquefied are Those Which are Absorbed in the Greatest Amount. CO_2, NH_3, and HCl are at once most easily liquefied and absorbed.

Oxygen, nitrogen, and hydrogen are liquefied with difficulty and are feebly absorbed.

(*b*) Different Liquids Absorb Different Quantities of the Same Gas. The *coefficient* of *absorption* (*a*) or the solubility of a gas is the volume of gas absorbed by a unit volume of the liquid at 0°C. and 760 mm. Note that (*a*) is determined for *constant temperature and pressure.*

$$a \text{ for } \frac{O}{H_2O} = \frac{0.0489}{1.00000}\ \frac{0.05}{1.00} \text{ or } 0.05\,;\ a \text{ for } \frac{CO_2}{H_2O} = \frac{1.7967}{1.0000}$$

$$\frac{1.8}{1.0} = 18\,;\ a \text{ for } \frac{N}{H_2O} = \frac{0.02348}{1.00000}\ 0.0235.$$

(*c*) The Amount of Gas Absorbed by the Same Liquid Varies with the Temperature.—The higher the temperature the smaller the amount of gas which may be held in solution, and conversely. Heating a liquid drives off much of the dissolved gas. One volume of H_2O, at 15° C. and 760 mm. pressure, absorbs of oxygen, 0.03415; of carbon dioxide, 1.002; of nitrogen, 0.01682 volumes.

(*d*) The Amount of Gas Absorbed by the Same Liquid Varies with the Pressure.—The higher the pressure of the gas above the liquid the greater the amount which will be dissolved by the liquid. If the pressure be relieved, as in the opening of a bottle of "soda-water," the gas (CO_2) escapes rapidly with effervescence. One volume of H_2O at 0°C. and $\frac{760 \text{ mm.}}{2}$ pressure will absorb of oxygen $\frac{0.0489}{2} = 0.0245$.

(*e*) The Absorptive Power of a Liquid for a Particular Gas is Independent of Other Gases Which it May Already Hold in Solution.—Thus a liquid in contact with a mixture of gases absorbs a quantity of each gas, just as if it were the only one present, the amount being determined by the coefficient of absorption, and the pressure of the gas in the mixture, or the Partial Pressure.

(*f*) Each Gas Forming a Part of a Mechanical Mixture Exerts a Partial Pressure Proportional to its Part of the Mixture.—Taking the proportions of the gases in the atmosphere, one concludes that as oxygen represents 20.96% (say 21%) of the mechanical mixture, its partial pressure would be 21% of the whole pressure, *i. e.*, 21% of 760 mm. mercury or atmospheric pressure. Partial pressure for oxygen in pure air is $.21 \times 760 = 158$ mm. mercury. Partial pressure for CO_2 in pure air is $.0004 \times 760 = 0.3$ mm. mercury. It is estimated that in the alveoli of the lungs the partial pressure for oxygen is 122 mm.; and for CO_2, 38 mm.

We may now make the following application of the foregoing principles: *The absorption of oxygen* by water (or blood plasma) at 0°C. and 760 mm. barometer pressure, with a partial pressure equal to 20.96% of an atmosphere equals: $a' = 0.0489 \times \frac{20.96}{100} = 0.01$, *i. e.*, 100 volumes of water or plasma would absorb under the conditions named about one volume of oxygen.

The *absorption of oxygen* at 37.5°C. and partial pressure = 20.96 per cent. of 760 mm. $a'' = 0.026 \times \frac{20.96}{100} = 0.0054 +$, *i. e.*, 100 volumes of water or plasma would absorb under the conditions named about one-half volume per cent. of oxygen.

The absorption of oxygen at 37.5°C. and partial pressure of the alveoli or 16 per cent. of 760 mm. $a''' = 0.026 \times \frac{16}{100} = 0.004 +$, *i. e.*, blood plasma at body temperature would absorb from the alveoli of the lungs 4 c. c. oxygen for every liter of plasma. If absorption of oxygen were to depend solely upon its physical relation to plasma this would be practically the limit of absorption.

The absorption of CO_2 at 37.5°C.[1] the partial pressure of CO_2 in the alveoli being 5 per cent. of 760 mm. $a''' = 0.569 \times \frac{5}{100} = 0.028 +$, *i. e.*, if in the alveoli of the lungs the atmosphere contains 5 per cent. of CO_2, 100 volumes of plasma would absorb 2.8 volumes of CO_2; or, in other words, CO_2 can, according to this course of reasoning, be diffused from the blood into the air passages only when the amount in the plasma exceeds 2.8 c. c. per 100 c. c. plasma. Furthermore, that this proportion would represent approximately the proportion of CO_2 in arterial blood, as far as it could exist under physical laws.

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[1] a for $\frac{CO_2}{H_2O}$ at 37.5°C. and 760 mm. = 0.569 volumes per cent.

THE PHYSIOLOGY OF RESPIRATION.

A. THE MECHANICAL AND PHYSICAL FEATURES OF RESPIRATION.

1. STRUCTURAL FEATURES.
    - *a.* Changes of Thoracic Diameters.
    - *b.* Muscles of Respiration.
2. OBSERVATION OF CHANGES IN THE DIAMETERS OF THE THORAX.
3. PHYSICAL EFFECTS OF THE CHANGES OF THE THORACIC DIAMETERS.
    - *a.* Intra-Thoracic Pressure.
    - *b.* Respiratory Pressure.
    - *c.* Intra-Abdominal Pressure.
    - *d.* Lung Capacity.
    - *e.* Types of Respiration.
    - *f.* Modifications of the Respiratory Act.

B. THE CHEMISTRY OF RESPIRATION.

1. EXTERNAL RESPIRATION.
    - *a.* Respiratory Changes in the Air Breathed.
        - (1) *Composition of the Normal Atmosphere.*
        - (2) *Qualitative Changes Produced by Respiration.*
        - (3) *Quantitative Changes of the Air in Respiration.*
    - *b.* Respiratory Changes in the Blood.
        - (1) *The Gases of the Blood.*
        - (2) *The Relation of Oxygen in the Blood.*
        - (3) *The Relation of Carbon Dioxide in the Blood.*
        - (4) *The Influence of Blood-Gases upon the Spectrum.*
2. INTERNAL OR TISSUE RESPIRATION.

A. THE MECHANICAL AND PHYSICAL FEATURES OF RESPIRATION.

1. THE STRUCTURAL FEATURES.

If the constituents of the atmosphere were compelled to make their way through the respiratory passages by simple diffusion the amount of oxygen received into the blood would at best permit a most sluggish katabolism. It may have been observed that the frog uses the floor of the mouth as a sort of bellows to pump air into the lungs, while an occasional spasmodic contraction of the body wall forces the air out. In birds the elastic bony thorax is compressed by muscles of the body walls; this action forces the air out of the lungs. Relaxation of the abdominal muscles allows the thorax to regain its original volume and air rushes in to fill the lungs. In mammals the condition is quite opposite. The inspiration representing the muscle-contraction and the expiration representing relaxation.

The anatomical characters of the mammalian thoracic skeleton, which are of especial importance physiologically, are: (I) The greater mobility of the posterior than the anterior part of the thoracic skeleton. (II) The posterior slant of the ribs. (III) The double vertebral attachment of the ribs, making an axis of rotation which does not coincide with the axis determined by the simple raising and lowering of the ends of the ribs. (IV) The noticeable angle which the fourth, fifth and sixth ribs make with their cartilages. (V) More important than any skeletal character is the fact that the thoracic cavity is separated from the abdominal cavity by a muscular partition which is very convex upward or anteriorly. When the radial muscle fibers of this diaphragm contract the arch is flattened, the contents of the abdomen pressed farther downward, the capacity of the thorax suddenly increased; but any increase in the capacity of the thorax must lead to a rarefaction of the air, or to negative pressure. This tendency to the production of negative pressure is speedily satisfied by the influx of air through the respiratory passages filling the lungs, which in turn fill the increased space of the thorax. Through the action of the diaphragm, then, the antero-posterior dimension of the thorax is increased.

a. The Changes of the Thoracic Diameters.

(*a*) THE ANTERO-POSTERIOR DIMENSION is actively increased by the contraction of the diaphragm and passively decreased by the relaxation of the diaphragm. It may be actively decreased by a contraction of the abdominal muscles, which forces the contents of the abdomen up against the diaphragm, distending its arch, thus further encroaching upon the thoracic cavity and forcing air out of the lungs.

(*b*) THE DORSO-VENTRAL DIMENSION is increased by the contraction of the external intercostal muscles. The mechanism of the movement is as follows: (I) Ribs more and more mobile from before backwards; (II) Ribs slant posteriorly; (III) External intercostals having their origin on the posterior margin of a rib, pass ventrally and posteriorly to be inserted upon the anterior margin of the next succeeding rib. With all of these peculiarities of structure a contraction of the external intercostals must result in an elevation of the ends of the ribs and a carrying of the sternum further away from the vertebral column. Still another factor in this is the opening of the angle between 4th, 5th and 6th costal cartilages and their ribs. The dorso-ventral dimension is decreased by the elasticity of the thorax which causes it to return to its former size on relaxation of the external intercostals.

(*c*) THE LATERAL DIMENSION.—By virtue of the double vertebral attachment of the ribs, mentioned above, the action of the external intercostals is not only to carry the end of a rib farther from the vertebral column as its general line approaches a position perpendicular to the spine but also to carry the middle of the rib farther from the median line of the thorax as the plane, which its curve determines, approaches the perpendicular to that line. It might at first be supposed that a contraction of the diaphragm would pull in the walls of the thorax, thus decreasing the lateral dimensions; but Brücke showed conclusively that though it undoubtedly exerts a strong tension on the thoracic wall the high-domed mass of abdominal viscera, upon which the force of the diaphragm is directly exerted, is pressed downward and outward against the upper abdominal walls and so neutralizes the tendency in the opposite direction.

b. The Muscles of Respiration.

1. **Muscles of Quiet Respiration.**—(*a*) Inspiration.—(i) The diaphragm; (ii) the M. levatores costarum longus et brevis; (iii) Mm. intercostales externi et intercartilaginei.

(*b*) Expiration.—Ordinary quiet expiration is non-muscular, depending upon the weight and elasticity of the tissues. Inspiration throws the tissues out of the position of rest and they fall or sink back to that position during expiration.

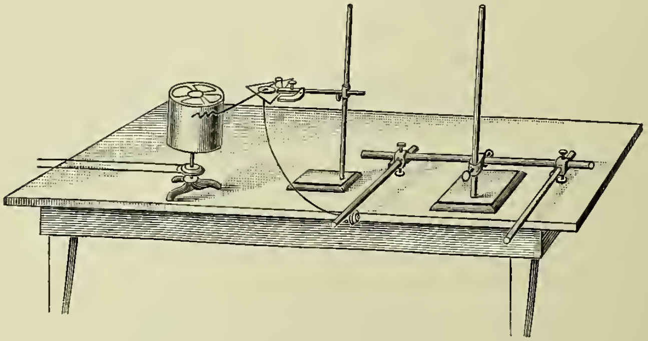
2. **Muscles of Forced Respiration.**—(*a*) Inspiration.—(*α*) Upper ribs raised by: (i) The three M. scaleni; (ii) M. serratus post. superioris; (iii) M. cervicalis ascendens. (*β*) Sternum is raised by: (iv) Musculus sterno-cleido-mastoideus; (v) M. sterno-hyoideus; (vi) M. sterno-thyroideus; (vii) M. thyro-hyoideus. (*γ*) The hyoid bone is raised by: (viii) M. mylo-hyoideus; (ix) M. stylo-hyoideus; (x) M. genio-hyoideus; (xi) M. digastricus. (*δ*) The shoulder girdle is raised and drawn backward by: (xii) M. trapezius; (xiii) Mm. rhomboidei, major et minor; (xiv) M. levatores anguli scapuli. (*ε*) Lower ribs drawn toward the raised and fixed upper ribs by: (xv) Pectoralis major et minor; (xvi) subclavius; (xvii) serratus magnus.

(*b*) Expiration.—(*α*) Abdominal contents compressed and forced against diaphragm by: (i) M. obliquus externus; (ii) M. obliquus internus; (iii) M. transversus abdominis; (iv) M. rectus abdominis; (v) M. levator ani. (*β*) Ribs are depressed by: (vi) M. rectus abdominis; (vii) M. quadratus lumborum; (viii) M. serratus posticus inferior; (ix) M. triangularis sterni.

2. OBSERVATION OF CHANGES IN THE DIAMETER OF THE THORAX.

The *observations* of the *dorso-ventral* and the *lateral diameter* are usually taken in the plane of the nipples or in the plane of the junction of the ninth rib with its costal cartilage. These thoracic planes must be taken perpendicular to the axis of the thorax.

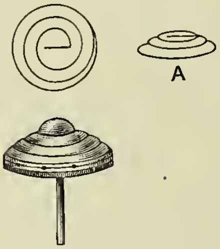
FIG. 123.



The stethograph.

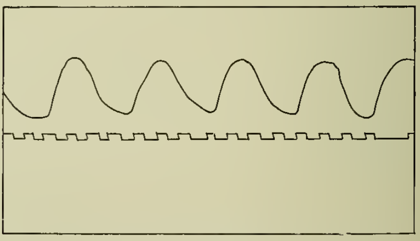
1. **The Calipers.**—This instrument is a most reliable apparatus for determining the diameter. As usually constructed, a graduated arc near the hinge of the instrument enables one to read off at once the number of centimeters between the points of the two limbs of the instrument. One may measure the dorso-ventral or the lateral diameter of the thorax when the thorax is in repose, or at the end of forced inspiration or of forced expiration. Such observations give not only the actual diameters, but the amount of expansion of the chest during the respiratory movements.

FIG. 124.



Stethograph tambour.

FIG. 125.



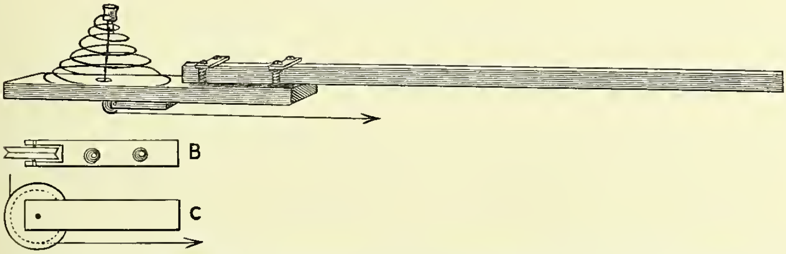
Normal stethogram of dorso-ventral diameter in nipple plane.

2. **The Stethograph.**—The accompanying figures (Figs. 123 and 124) show a convenient form of this instrument. As the name suggests, the purpose of this instrument is to record the movements of the chest. Recourse is had to the tambours. Fig. 124 shows the receiving tambour, whose membrane is held in a conical position by the spiral spring (A). The button of the receiving tambour follows the movements of the chest wall; the changes of pressure in the receiving tambour are communicated through a rubber tube, and the record is received upon carboned paper. Fig. 125 gives a normal stethogram. Note (1) that the rise

(inspiration) is more rapid than the fall (expiration); that (II) both inspiration and expiration are more rapid at first and gradually slow off at the end of the act; (III) that there is a moment between the acts when there seems to be no movement at all; (IV) that this moment of perfect inactivity is longer at the end of expiration than at the end of inspiration.

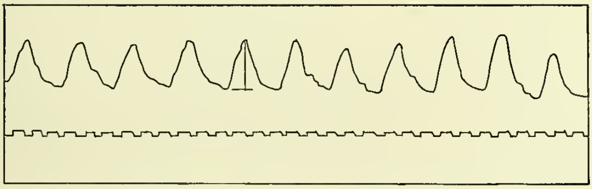
5. **The Thoracometer.**—This instrument not only traces a stethogram but the height of the waves bear an accurate and unvarying ratio to the movements of the chest wall. The instrument is used for quantitative work upon the thorax. The instrument consists of a thoracic frame similar to that of the stethograph shown above, but the rod which holds the receiving tambour is replaced by the rod shown in Fig. 126. The essential features of the thoracometer are: (I) a spiral spring fitted with a button which follows the movements of the chest wall; (II) an inelastic cord to transmit the movements of the button to a recording lever which, by weight or spring, is brought back to normal after being displaced by a movement of the button; (III) pulleys for changing the direction of the cord; (IV) a recording lever fitted with a tracing point; (V) a carboned drum for recording the movements of the lever. The arms of the lever being known the relation of the height of the wave to the actual movements of the chest may

Fig. 126.



Thoracometer attachment to the stethograph. The thoracometer differs from the stethograph in the substitution of this rod and spring for the rod and tambour of the stethograph. The cord which runs over the thoracometer pulley (B, C) passes to the writing lever.

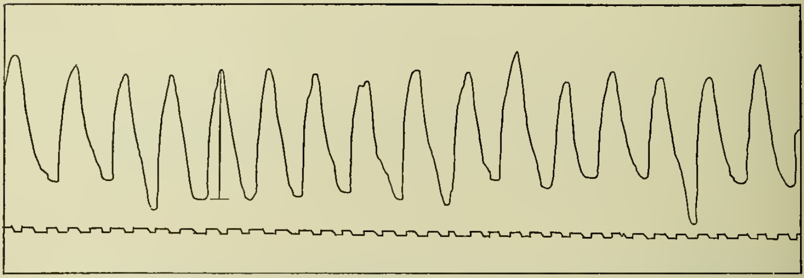
Fig. 127.



Tracings taken with the thoracometer. The ratio of the short to the long arm of the tracing lever being 0.25 the actual height of these waves multiplied by that *constant* will give the movement of the thoracic wall. Showing variation of lateral diameter at 9th rib, during quiet breathing. The height of the measured wave is 8 mm., the constant 0.25, the lateral diameter changed 2 mm.

be determined. Figs. 127 and 128 show two thoracometer tracings; both in the plane of the junction of the ninth rib with the costal cartilage. From the recorded observations one may draw the following conclusions: (I) the dorso-ventral diameter varies more than the lateral diameter, expanding normally about two or three times as much as the latter; (II) successive respiratory acts differ, some being beyond the average in depth of inspiration and some beyond the average in extent of expiration.

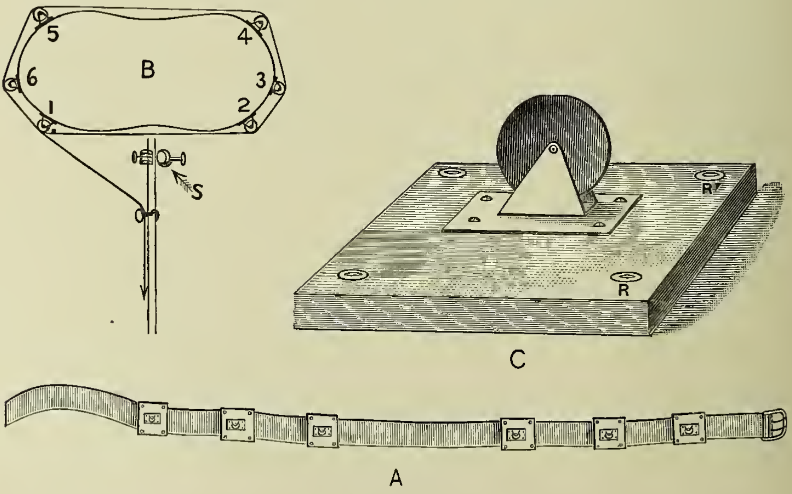
Fig. 128.



Showing variation of dorso-ventral diameter at plane of 9th rib, during quiet breathing. The height of the measured wave is 20.5 mm., the constant 0.25; the dorso-ventral diameter changed 5.12 mm. during the act whose record is measured.

4. **The Belt Spirograph.**—Various forms of the belt spirograph or pneumograph have been devised to give variations in the circumference of the thorax. Most of these devices are modeled after Marcy's pneumograph, which consists of a cylindrical tambour with membranous end. From the two ends of

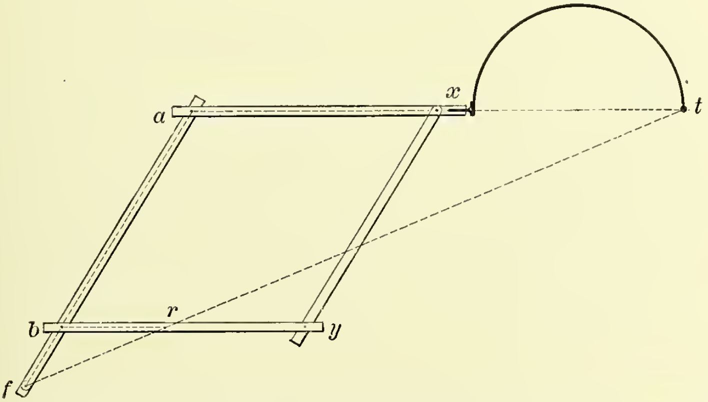
Fig. 129.



The belt spirograph.

the cylinder an inelastic cord girths in the chest. Increase of the girth extends the membranous end of the cylinder, lowers the pressure in the cylinder, while a decrease in girth increases the pressure in it. Thus the changes in circumference incident to respiration may be recorded. Like the spirograph the pneumograph of Marey is reliable only for showing qualitative changes of the circumference. If one wishes to measure these changes it will be necessary to use some such instrument as the one here figured (Fig. 129). In the figure *a* is an elastic belt having pulleys which are adjustable along the belt. The pulley is shown in C. Fig. 129, B, shows a plan of the thorax with the belt adjusted. An inelastic cord, tied into an eye in pulley No. 1, passes around the chest over pulley No. 1 and one or two other pulleys to change the direction, finally passing to a recording lever adjusted like the one used with the thoracometer. Changes in girth are very accurately recorded by this device.

FIG. 130.



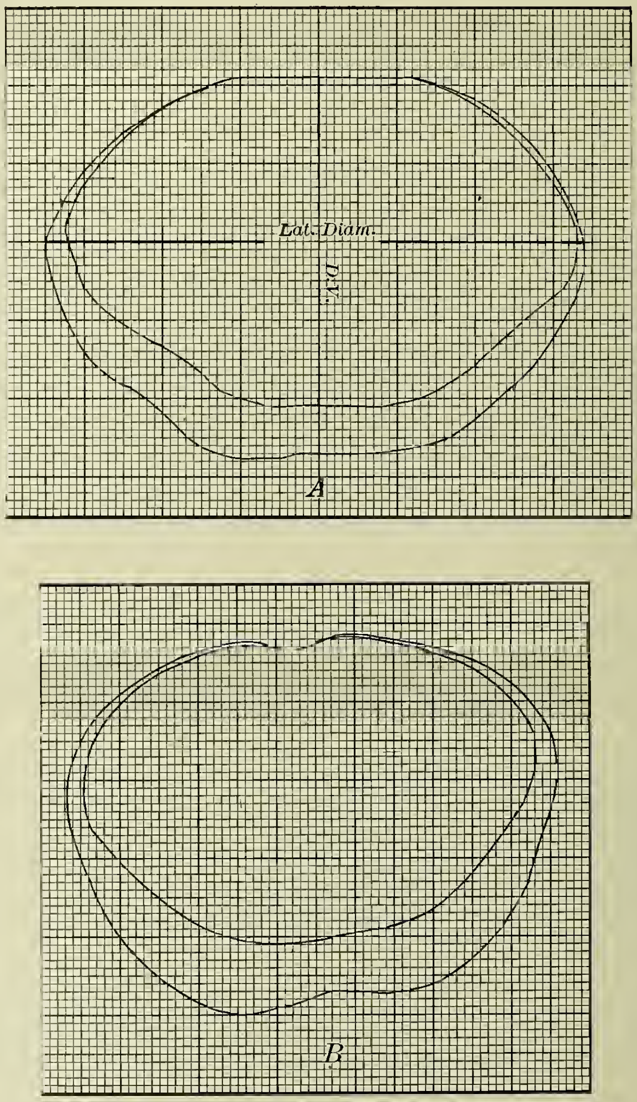
The chest pantograph. For measuring and recording *chest contours*. The instrument is constructed of brass or of wood with brass or steel semi-circle. The joints *a*, *b*, *x*, and *y* move easily in the plane of the instrument. The semi-circle, 40 in. in diameter, rotates at *x* around the diameter *t x*. The point *f* is fixed to a table. With *f* a fixed point all movements of *t*, the tracing point, are accompanied by corresponding movements of *r*, the recording point. The triangle *f r b* and *f t a* are similar triangles in all positions of the instrument $fb : fa :: fr : ft$; but $\frac{fb}{fa} = \frac{1}{5}$; therefore, the distance *fr* is always $\frac{1}{5}$ the distance *ft*.

Study of tracings justifies the following conclusions: (I) The respiratory acts—as indicated in the change in girth—are not uniform, an occasional one—every eighth to twelfth—being much more extensive in inspiration, sometimes followed by one or two somewhat deeper in expiration. (II) Variation in rate of inspiration accompanies the variation in extent of the inspiratory or expiratory acts.

5. **The Chest Pantograph.**—This instrument in tracing upon "millimeter" or "ordinate" paper an outline of the thorax at any

level enables one to determine quantitatively not only any diameter but the area also, as well as any peculiarities of sectional contour.

Fig. 131.



Contours of chest, taken with chest pantograph.

Just this feature of the instrument enables it to do what the other appliances above decribed fail to do. For description of this instrument see explanation of Fig. 130. If the subject to be examined sit beside a table on which the instrument is fixed; if the seat be adjusted in height to bring the plane of the thorax to be examined into the plane of the instrument, *i. e.*, on a level with the top of the table; if a sheet of millimeter paper be fixed to the table under the recording pencil *r*; and if the tracing point *t* be swept around the thoracic wall a record of the chest contour will be traced upon the paper. The accompanying Fig. 131 shows two such contours from healthy well-developed young men. Two millimeters in the figure equal one centimeter of actual measurement. The inner contour is that of forced expiration while the outer one is that of forced inspiration. In contour *A* the increase of lateral diameter by forced inspiration is 2 cm. while the increase of dorso-ventral is 3 cm. In the same contour the cross sectional area of the thorax in the plane of the ninth rib is represented by 25.52 of the larger squares containing 25 square cm.; total area = 637.5 square cm. while the cross sectional area of the chest in forced expiration is 517.5 square cm. Forced inspiration shows an increase of 120 square cm. or about 23 per cent. over cross section area of forced expiration. Furthermore, both contours show a prominence on the right side (left in the figure) possibly due to stronger musculature on that side.

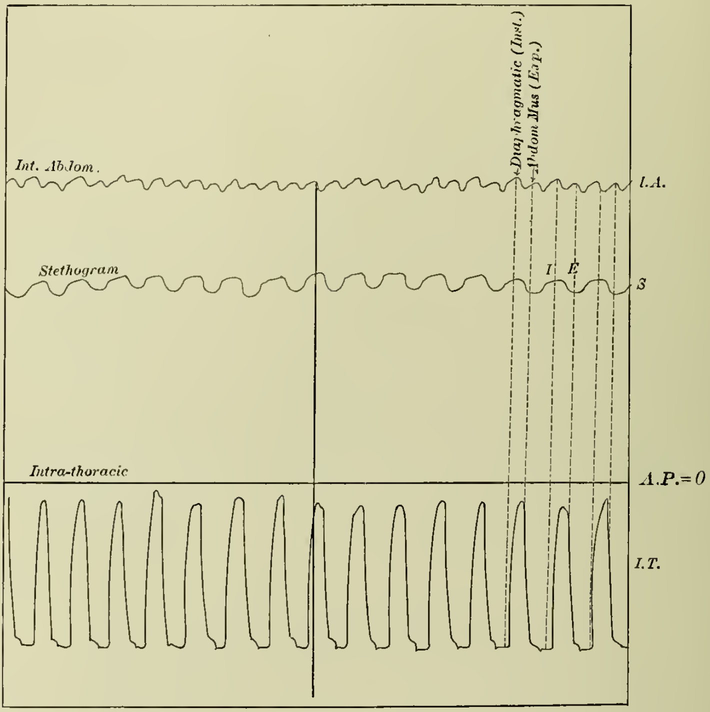
3. THE PHYSICAL EFFECTS OF THE CHANGES OF THE THORACIC DIMENSIONS.

a. Intra-thoracic Pressure.

Intra-thoracic pressure is the pressure in the thoracic cavity outside of the air passages; that is in the pleural and mediastinal cavities especially, though it affects the blood and lymph vessels of the thorax which are not in either of the two cavities mentioned. If one introduce into the pleural or the mediastinal cavity a cannula whose external end communicates through a tube with a recording tambour or with a manometer it will be found that there is a fall of the recording lever or of the mercury, indicating a fall of pressure below the atmospheric pressure. It fact, the recording lever or the mercury will not again rise to the level of atmospheric pressure; but will oscillate up and down below the zero line, being lower during inspiration than during expiration. Fig. 132 gives a tracing of intra-thoracic pressure (*I. T.*), atmospheric (*A. P.*), intra-abdominal pressure (*I. A.*) and a stethogram (*S.*). The tracings were taken from a rabbit under ether, and are simultaneous. The thing which must be first established is the relation between the intra-thoracic pressure and the respiratory movements. When the chest wall rises in inspiration—tracing *S*, phase *I*—note that the thoracic pressure falls to the minimum;

when the chest wall falls in expiration (S–E) the intra-thoracic pressure reaches a maximum. This maximum does not reach the

FIG. 132.



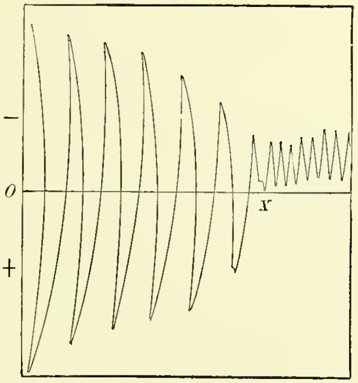
Simultaneous tracings of intra-thoracic pressure. (*I.T.*), intra-abdominal pressure (*I.A.*) and a stethogram.

zero-line under ordinary circumstances. That is, *intra-thoracic pressure is always negative, but it is more negative during inspiration than during expiration.* If the lungs were inelastic sacs the pressure between the lungs and the thoracic wall—intra-thoracic—pressure would become zero almost instantly on the cessation of the inspiratory act. But while the thoracic wall is by its elasticity regaining its original position of repose at the end of expiration the elastic sacs within the thorax are contracting by virtue of their elasticity. Now, inasmuch as the elasticity of the lungs had to be overcome by the negative pressure outside of them it is easy to see that when there is no obstruction to the exit of air from the lungs they will tend to assume their position of repose more quickly than will the thoracic wall, that is, they will tend to pull away from the thoracic wall, leaving a negative pressure in the pleural cavity.

Intra-thoracic pressure may be positive if there is a forced expiration with occluded exit of air; or in a quick expiration with a partial obstruction to the free exit of air the pressure in the pleural cavity will be positive. In Fig. 133 the nostrils of the rabbit under observation were held shut at *x*. The vigorous respiratory acts which the animal made in its effort to get air made the inspiratory pressure much lower than usual and the expiratory pressure much higher than usual, reaching almost as far on the positive side of the zero line as on the negative side.

Physiologically the intra-thoracic pressure is positive during the forced expiration of coughing, sneezing, and straining at stool, or lifting. The face becomes red in the two last because the positive pressure is sustained, blocking venous flow to the heart.

Fig. 133.



Tracing of intra-thoracic pressure showing influence of an obstruction in the air passages introduced at *X*.

b. Respiratory Pressure.

Respiratory pressure is the pressure in the air passages. It is always negative during inspiration and always positive during expiration. If it were not negative during inspiration the air would not flow into the lungs and if it were not positive it would not flow out of the lungs during expiration. In quiet breathing the respiratory pressure is only slightly positive and slightly negative. Should the air-passages become partially obstructed as in sneezing, or coughing, the positive pressure of expiration may be very high. During lifting or straining at stool the positive pressure in the air

Fig. 134.

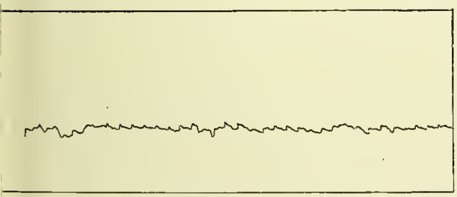
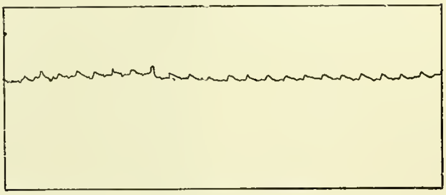


Fig. 135.



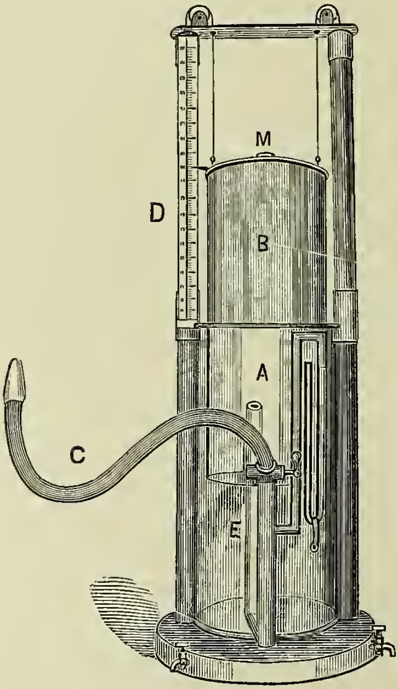
Cradio-pneumatograms showing influence of the pulsation of the thoracic arteries upon respiratory pressure.

passages exceeds the positive pressure in the pleura by the amount of the elasticity of the lungs. If one hold in the mouth or nose a tube whose distal end is connected with a recording tambour one will notice that the recording lever rises and falls synchronously with ventricular systole, or with the pulsations of the thoracic arteries. To successfully trace this "cardio-pneumatogram" one must either breathe very quietly or suspend respiration altogether for short periods during which the tracing may be taken. Note in the accompanying tracings indubitable evidence of systolic and dicrotic pulse waves which have been transmitted through the air of the respiratory passages and thence to the recording lever via the tambour and tube.

c. Intra-abdominal Pressure.

Intra-abdominal pressure is zero or very near zero ± at the end of expiration in quiet breathing; that is, when thoracic and abdominal walls are in a state of perfect repose. When the diaphragm descends in inspiration the pressure becomes decidedly positive, forcing abdominal viscera and wall outward against atmospheric pressure. (See Fig. 132, *I. A.*) If the viscera and wall regain their position of repose in response to the elasticity of the abdominal wall there will be but one wave of positive pressure and that is caused by the descent of the diaphragm, and occurs when intra-thoracic pressure is lowest. If there is an active contraction of abdominal muscles—as in the case in Fig. 132—there will be a second rise of pressure due to that contraction, and it will occur during expiration. These relations are well shown in the tracing. The influence of intra-abdominal pressure upon venous and lymphatic circulation has been discussed above. Coughing and sneezing cause a sudden positive pressure of moderate degree, but straining at stool, lifting, and straining in parturition

FIG. 136.



Hutchinson's spirometer.

cause a sustained positive pressure of high degree, and a consequent forcing of blood and lymph already in large abdominal vessels into the thorax, but a blocking of any further entrance of venous blood or of lymph into the abdomen, thus backing it up in the veins of the lower extremities.

d. Lung Capacity.

This expression is used to indicate the quantity of air flowing into or out of the lungs during respiration. The instrument used to measure the air is called a *Spirometer.* If the air is collected over water it is a *Wet Spirometer* (see Fig. 136), if in an elastic bag, a *Dry Spirometer.* The results obtained from observations will vary within wide limits and according to the combination of several factors, *e. g.*, stature, girth of chest, muscular development, habits, age, sex, accumulation of fat, etc., etc. If an average-sized man, of average muscular development, breathe quietly into a spirometer it will be observed that only 300 to 500 c.c. flow into and out of the instrument with each respiration. This quantity of air involved in normal quiet respiration is called TIDAL AIR. The quantity will vary from 300 c.c. in perfect rest to 500 c.c. or more, during or just after moderate exercise, as walking.

But if the exercise be more than the most moderate, the respirations will deepen until the tidal air may reach 1,000 c.c., or even more. If 500 c.c. be arbitrarily assumed as tidal air, then the excess which may be inspired in forced inspiration is called COMPLEMENTAL AIR, and for men of average stature and development this will approximate 1,600 c.c. If at the end of such a forced inspiration an expiration is begun which empties out the 1,600 c.c. and the 500 c.c., it will be found that the muscles of

FIG. 137.

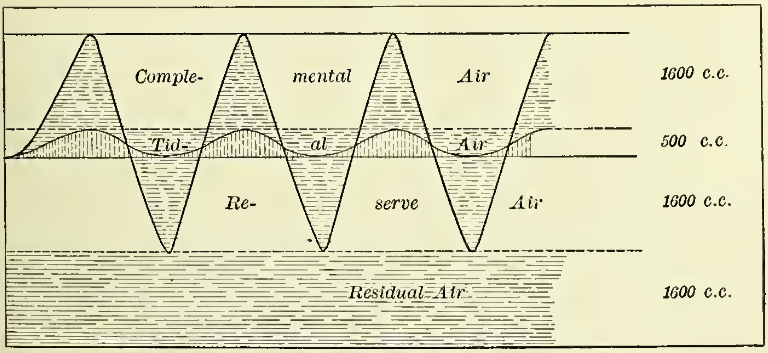


Diagram of lung capacity.

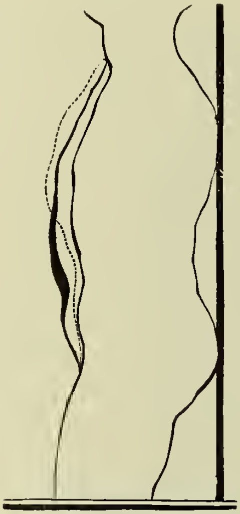
forced expiration can force out still more air to the extent of another 1,600 c.c. This last air of forced expiration is called RESERVE AIR. The total quantity expired after forced inspiration is called VITAL CAPACITY and is the sum of the tidal, complemental and reserve (500 + 1,600 + 1,600 = 3,700 c.c.). But at the end of forced expiration the lungs are not empty. There still remains a so-called RESIDUAL QUANTITY, which is estimated at 1,600 c.c. It is an accidental forcing out of a part of this residual air that causes such inconvenience when one gets a forcible and unexpected thump on the thorax.

A diagram representing these terms and definitions will be found in Fig. 137.

e. Types of Respiration.

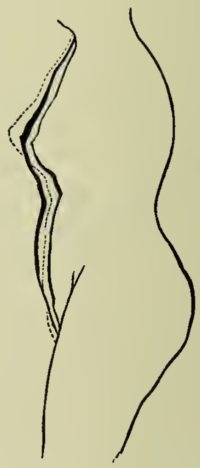
1. Diaphragmatic, Inferior Costal and Superior Costal Types.—An infant breathes almost exclusively by means of contractions of the diaphragm. The flattening of the arch of the diaphragm presses upon the abdominal viscera and pushes out the abdominal walls; this type of respiration is called *abdominal* or *diaphragmatic*. At about the age of puberty there is, in all European races at least, a distinct difference in the male and female respiratory movements. (See Figs. 138 and 139.) The narrower, continuous, ventral line shows the position of repose, the heavier, continuous line shows the position at the end of medium inspiration. Note that in the

FIG. 138.



The changes of the thoracic and abdominal walls of the male during respiration.

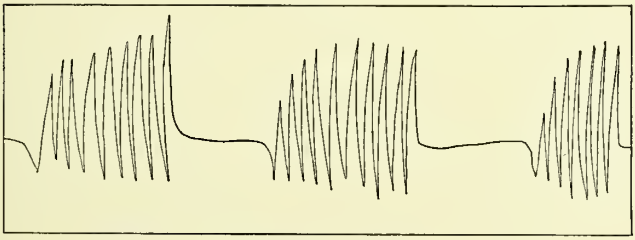
FIG. 139.



The same in the female. (HUTCHINSON.)

male the line is somewhat further advanced in the lower costal and abdominal regions than is the case in the female, while in the female the upper costal region is advanced relatively further. These two types are called respectively the inferior costal and superior costal type. Note that in deep inspiration, shown in the interrupted line, the inferior costal type of the male is more pronounced, *i. e.*, in deep inspiration the 9th rib girth expands most in the male, while it is the girth in the nipple plane which expands most in the female. There has been some controversy as to the reason for this difference. Is it fundamental or incidental? Is it due to sexual life; viz., child-bearing in the female? If so, all women of all races should show it. Some authorities (Mays and Kellogg) say that the American Indian women and Chinese women do not show the superior costal type of breathing, and, therefore, the difference must be incidental and probably depends upon dress.

FIG. 140.



Cheyne-Stokes respiration.

2. **The Cheyne-Stokes Type of Respiration.**—The accompanying figure represents a stethogram with a slowly rotating drum. Note the series of rather rapid, deep respiratory movements alternating with perfect rest in the recorded case above. Sometimes, however, there is an alternation of a series of deep with a series of shallow respirations. In the latter form it is frequently to be noticed in children during sleep. It is seen in chloral poisoning, morphine poisoning and in nervous diseases which interfere with the action of the center. The Cheyne-Stokes respiration in its physiologic forms seems to bear to respiration a relation analogous to that which the Traube-Hering pressure curves bear to circulation, both rhythms originate in the medullary centers; the first governing respiratory rhythm and the second governing vaso-constrictor tonus. The cycle of the Cheyne-Stokes movement is repeated once to three times per minute.

f. Modifications of the Respiratory Act.

1. **Coughing.**—When the respiratory mucous membrane, in or below the larynx, is irritated by inhaled dust, or gases or by ex-

uded secretions—mucus or muco-pus—the system makes an effort to expel the offending substance by a forcible expiration accompanied by a closure of the larynx followed by its sudden opening and an explosive expulsion of the air in the upper air passages this blast of air usually carries with it the irritating matter.

2. **Sneezing.**—When the nasal mucous membrane is irritated in any way a similar expulsion of the air through the nose serves to remove the irritating matter. Both coughing and sneezing are preceded by an inspiration of more than usual depth.

3. **Yawning.**—If for any reason the respiration has fallen behind the requirements of the system for oxygen there is an involuntary effort on the part of the respiratory system to make the deficiency good. This is accomplished through a prolonged and very deep inspiration, followed by a very complete expiration and this in turn followed by a rather deep inspiration after which the respiration proceeds in the usual quiet rhythm.

4. **Hiccoughing.**—Hiccough consists in a sudden contraction of the diaphragm which causes a spasmodic inspiration ; this is blocked by the sudden closure of the glottis, causing the characteristic sound. Certain kinds of gastric irritation, especially the taking of dry food or the mechanical irritation which the stomach undergoes incident to inordinate laughing where it is subjected to a series of quick pressures by the abdominal muscles. In the first case a drink of water usually stops the hiccough, in any case it is likely to stop if the attention is either closely fixed upon it or completely diverted from it.

5. **Sighing.**—Sighing is very similar to yawning in its mechanism except that its cause is due primarily to the emotions. Grief, sorrow and even extreme fatigue may be accompanied by sighing.

6. **Crying and Laughing.**—These are purely emotional in their origin and consist of a deep inspiration (in crying) usually followed by a series of spasmodic vocalized expirations (in laughing usually). But crying and laughing are subject to so many individual peculiarities in sound and in facial expression that it is impossible to draw a distinct picture of either or a definite line between them.

7. **Sobbing.**—After prolonged crying the respiration is likely to take the form of sobbing which is a series of convulsive inspirations accompanied by partial closure of the glottis.

B. THE CHEMISTRY OF RESPIRATION.

1. EXTERNAL RESPIRATION.

a. Respiratory Changes in the Air Breathed.

1. **Composition of the Normal Atmosphere.**—The open atmosphere is a mixture of gases in the following approximate proportions :

Atmosphere	Nitrogen, including Argon, etc.,	79.00	in 100 parts.
	Oxygen,	20.96	
	Carbon dioxide,	0.04	

NH_3, H_2O; organic matter, in small variable quantities. Though the quantity of H_2O in the air is considerable—over 1 per cent.—it is not customary to reckon it in the gaseous constituents. How is the air changed during its stay in the lungs? An apparatus may be constructed which will show both qualitatively and quantitatively the principal changes effected. If a small animal be confined in a sealed chamber and provided with dried air which has been deprived of all CO_2 it will be found that the air on leaving the chamber has received considerable CO_2 and H_2O and a small amount of organic matter and that it has a higher temperature. Systematically enumerated the changes in respiration are:

2. **Qualitative Changes Produced by Respiration.**—(*a*) CHANGE OF TEMPERATURE.—Air below 36° C. would always be increased in temperature, though not quite to blood temperature, 38° C. In ordinary quiet respiration of air at ordinary room temperature (20° C.) the expired air has a temperature between 36° C. and 37° C. Very cold air would not be raised to that temperature, and very warm air (40° C.) would not be lowered to that temperature.

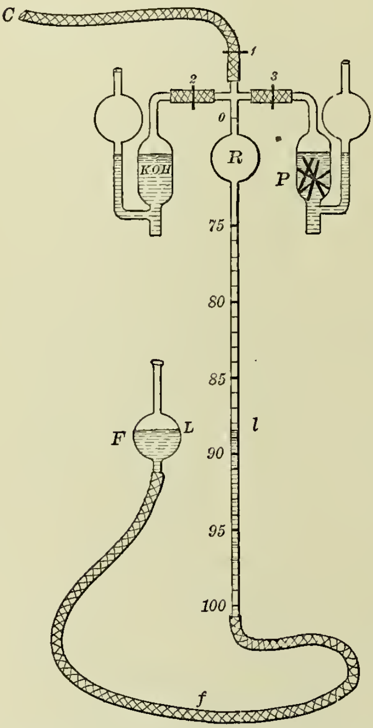
(*b*) CHANGE IN PROPORTION OF CO_2.—The CO_2 is always increased. If the inspired air be pure the expired air will contain 4 per cent. to 5 per cent. (4.34 per cent.) CO_2.

(*c*) CHANGE IN PROPORTION OF OXYGEN.—The oxygen is always decreased. If the inspired air be pure, *i. e.*, has 20.96 per cent. oxygen, one-fourth of the oxygen is consumed at one breathing of the air. With successive re-breathing less and less oxygen is consumed, but eventually it can all be taken out of the air, leaving the latter quite free of oxygen and composed of 79 per cent. of nitrogen; CO_2, H_2O, etc., 21 per cent.

(*d*) CHANGE IN VOLUME.—If the volume of inspired air be compared with that of the expired air it will be found that it is greater; but we must not forget that the expired air has a higher temperature, and that increase in temperature makes a marked difference in the volume of gases. If we reduce it to the same temperature it will be found to have actually decreased slightly in volume. Now, one liter of oxygen, combined with carbon, makes one liter of carbon dioxide at the same temperature and pressure. If the oxygen of the inspired air has all combined with carbon, why should there be any decrease in volume? But the oxygen of the inspired air does not all combine with the carbon; some of it combines with hydrogen to form H_2O, and that causes the difference in volume.

(*e*) CHANGE IN THE PROPORTION OF WATER.—The water is generally increased, though it may be decreased. Though the cool inspired air may be saturated with water at that temperature, the raising of the temperature in the air passages increases the capacity of the air for water and more is taken up from the moist mucous membrane. If warm air is saturated with moisture before entering the lungs it will take up very little more. If warm air be dry—the usual condition in furnace-heated houses—it will take up moisture very rapidly from the nasal passages and trachea and upper bronchi. This is irritating to the delicate membranes and is one of the many causes for catarrh.

FIG. 141.



Apparatus for estimation of O and CO_2 in expired air. (After WALLER.) *R*, a 100 c.c. receptacle graduated to one-tenth c.c. between 75 and 100; *F-f*, Filling flask and tube for filling and emptying receptacle; *C*, Connecting tube with screw clips at 1, 2 and 3; *KOH*, absorption flask for CO_2 containing a strong solution of potassium hydrate; *P*, absorption flask for O, containing sticks of phosphorus in water. In using the apparatus the filling flask is (I) filled with acidulated water and raised till the liquid stands at 0; (II) open clip 1; lower *F* to draw in 100 c.c. of expired air; (III) close 1, open 2, raise *F* till liquid rises to 0, close 2, under the pressure the *KOH* absorbs the CO_2 in one or two minutes; (IV) Drop *F* till the liquid in *F* (*L*) has the same height as *l*; read loss in volume of gas; this loss is the CO_2 absorbed by *KOH*; (V) open 3; raise *F* till *l* stands at 0; close 3; the phosphorus absorbs the oxygen in a few minutes; (VI) lower *F* till *L* and *l* are in line and read off loss of volume in oxygen.

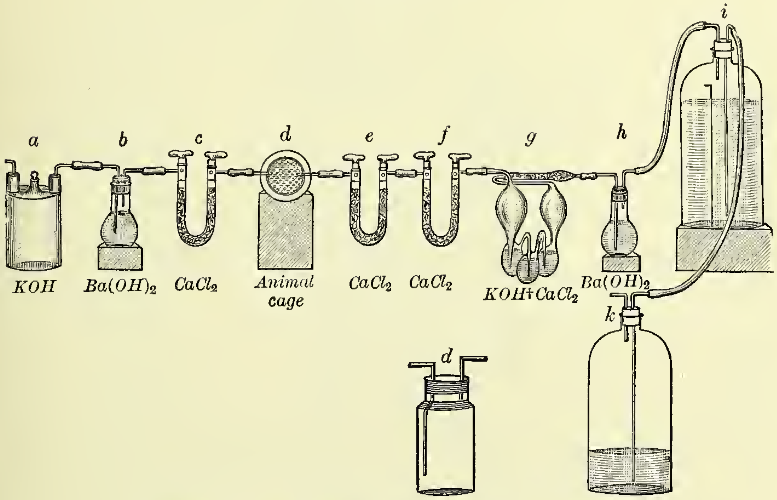
(*f*) ORGANIC MATTER in minute quantities is added to the air in the lungs.

3. **Quantitative Changes of the Air in Respiration.**—(*a*) THE ESTIMATION OF THE OXYGEN AND CO_2 IN EXPIRED AIR.—The accompanying Fig. 141 shows a very efficient and simple appliance for the determination in question. The expired air analyzed should represent the well-mixed product of many expirations. This may be accomplished by inspiring from the open atmosphere and expiring into a spirometer or similar receptacle. After sufficient time has elapsed for complete diffusion of the gases and cooling to room temperature 100 c. c. may be drawn off and analyzed. Finally a correction must be made for temperature and pressure and all corrected readings given for 0°C. and 760 mm. pressure. The quantity of oxygen and of CO_2 in the open atmosphere may be determined as a preliminary step in the experiment.

The above described observation gives the oxygen and CO_2 which exist after a single respiration of the air. From the data the amount of CO_2 added in a given time to the air in respiration may be fairly accurately determined.

(*b*) ESTIMATION OF CO_2 AND H_2O EXHALED.—A simple apparatus for accomplishing this is shown in Fig. 142. The general construction is as follows : (*d*) An animal-cage for which, for small animals, like rats or guinea-pigs, a large, wide-mouthed bottle may be used, (*a*) KOH; (*b*) $Ba(OH)_2$; (*c*) $CaCl_2$, free the afferent current of air of all CO_2 and H_2O, so that the animal inspires an atmosphere of nitrogen and oxygen in proportions that may be accurately determined; (*e*) and (*f*) are calcium tubes for absorption of the water, the increase in weight is equal to the water which leaves the animal cage during the experiment; (*g*) is a Geissler potash bulb for absorption of CO_2, its weight is taken before and after the observation; the $Ba(OH)_2$ flask (*h*) indicates whether all of the CO_2 has been absorbed by the potash bulbs; (*i–k*) is a siphon apparatus for drawing the air through the apparatus. The 10-liter bottles are graduated so that the quantity of expired air may be determined. The amount of oxygen in this expired air may be determined as above shown, and by taking the weight of the animal cage with and without the animal before and after the experiment we have data for determining: (I) The amount of oxygen consumed per kilogramme animal per hour; (II) the amount of CO_2 and of H_2O excreted per kilogramme per

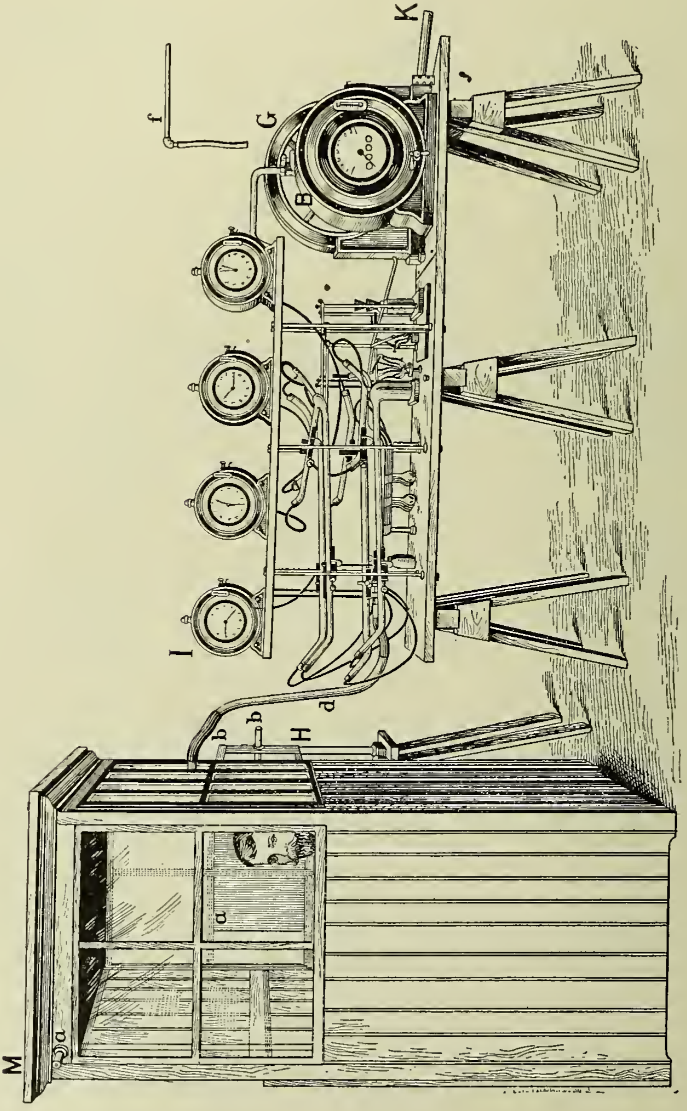
FIG. 142.



Apparatus for the extimation of CO_2 and H_2O in exhaled air.

hour. Unless the experiment is continued over considerable time the water excretion is only approximately determined. If there is no micturation or defecation by the animal the difference of

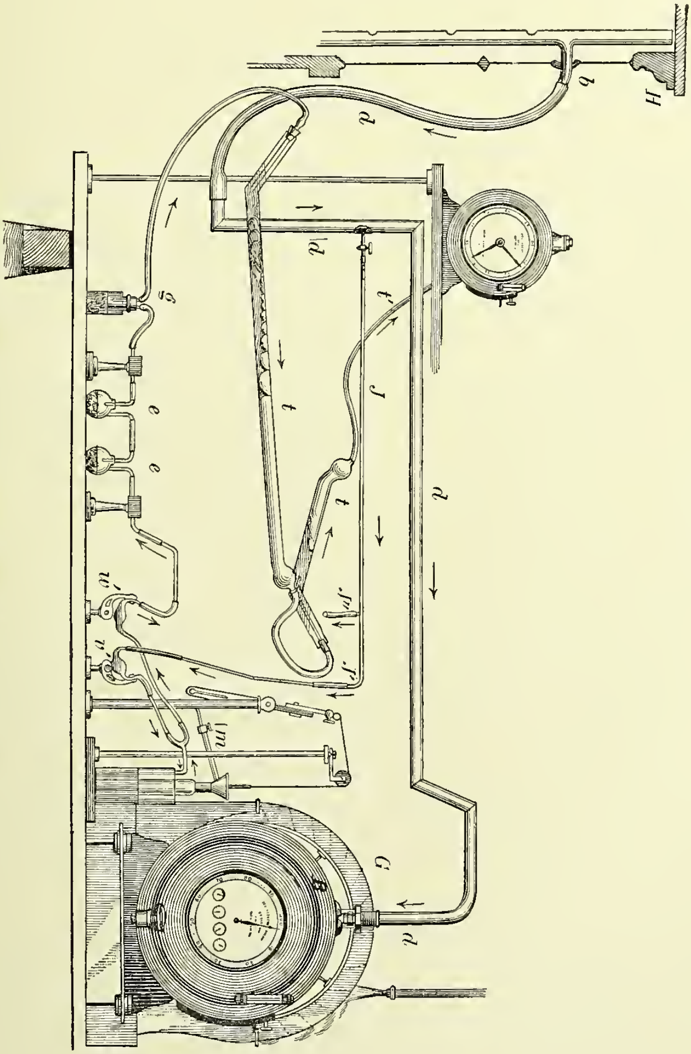
Fig. 143.



Voit's respiration apparatus.

weight in the calcium tubes will give the water excreted by lungs and skin. If there is micturation, a part of the water caught by the tubes will have been evaporated from the urine. If the animal be introduced into the cage just after voiding the urine, and if the amount of urine in the bladder at the end of the observation be determined it will be possible to make a fairly accurate estimate of the amount of water excreted during the period of observation.

Fig. 144.



Illustrating the connection of the tubes with one meter only. Lettering same as in Fig. 143.

When it is desired to observe the respiration of a man or larger animal one uses such an apparatus as that shown in Fig. 143, as elaborated by Voit and his pupils in Munich. The second figure (Fig. 144) gives the plan of the apparatus. A small portion of the air which passes through the respiratory chamber is diverted through the small tube *J*. The pump and valve apparatus at *m* and *w'* need not be described. At *e e'* the H_2O is absorbed by the H_2SO_4 and at *t*, *t'* the CO_2 is absorbed by $Ba(OH)_2$. The small gas meter beyond measures the quantity thus analyzed. Several portions are usually diverted through duplicate apparatus. (See Fig. 143.) All air not analyzed is measured by the large gas meter (*G*). This apparatus enables one to determine for a large animal or for a man the respiratory relations under various circumstances: (I) Rest; (II) work; (III) fasting; (IV) various diets; (V) drugs, etc.

(*c*) THE RESPIRATORY QUOTIENT.—This is the ratio between the volume of CO_2 exhaled and the volume of oxygen absorbed in the lungs. In the human subject, on an average diet, the air loses by absorption in the lungs 4.78 volumes per cent. of oxygen and receives from the blood 4.34 volumes per cent. of CO_2; hence the respiratory quotient: R. Q. $=\frac{CO_2}{O_2}=\frac{4.34}{4.78}=0.901$.

The respiratory quotient varies considerably in different *species*, and in the same animal under different conditions. Just how these variations arise will be made clear if we study the relation of these two gases in a combustion. If one liter of oxygen at 0° C. and 760 mm. pressure unite with carbon to form CO_2 that gas at 0° C. and 760 mm. will measure exactly one liter, so that the combustion quotient of pure carbon is $\frac{1 \text{ vol.}}{1 \text{ vol.}}=1$. Suppose now that we burn starch or cellulose, or any carbohydrate. Six molecules of oxygen (O_2) will unite with each molecule of carbohydrate to form six molecules of CO_2 and release the five molecules of H_2O. But the H_2O is not taken into account in combustion quotients or respiratory quotients; so that the combustion quotient of a carbohydrate would be $\frac{6CO_2}{6O}=1$. It must be evident that in the oxidation of carbohydrates in the animal organism the ratio would be the same, *i. e.*, R. Q. for carbohydrates $=\frac{6CO_2}{6O_2}=1$.

In the combustion or in the metabolism of fats the ratio is modified by the presence of a quantity of hydrogen whose oxygen is not provided for by the oxygen present in the fat molecule. Let us take tripalmitin as an example: Its formula is $C_3H_5[CH_3\cdot(CH_2)_{14}\cdot COOH]_3$ or $C_3H_5(C_{16}H_{31}O_2)_3$ or $C_{51}H_{98}O_5$. To oxidize the tripalmitin molecule it will require $51O_2$ to form $51CO_2$; but to oxidize the hydrogen of the molecule it will require 49 atoms of oxygen, six of which already exist in the molecule, leaving 43 atoms or 21.5 molecules to be supplied; $(51 \times 21.5 = 72.5)$; it will require then a total of 72.5 molecules of oxygen to yield 51 of CO_2, the combustion quotient or the R. Q. for tripalmitin $= \frac{510\,CO_2}{725\,O_2} = 0.7034$. The respiratory quotient for proteids can not be so accurately determined but it ranges for different proteids between 0.75 and 0.81.

From what has been said it is evident that the variations of respiratory quotient must vary with the proportion of carbohydrates, fats, and proteids in the diet: (I) in herbivora, R. Q. = 0.9 to 1.0; (II) in carnivora, 0.75 to 0.80; (III) in omnivora, 0.80 to 0.90. During fasting the animal consumes its own tissues;—*i. e.*, the reserve fats and proteids—and the respiratory quotient ranges from 0.70 to 0.75. In the child the respiratory quotient is lower than in the adult, due undoubtedly to the more active proteid metabolism in the growing individual. The ratio is higher in the daytime than at night, because the muscular activity is greater during the day and muscular activity is accompanied by a free katabolism of dextrose (carbohydrate) in the muscle while the muscle tissue itself (proteid) is katabolized no more during work than during rest.

The following table illustrates some of the points mentioned above:

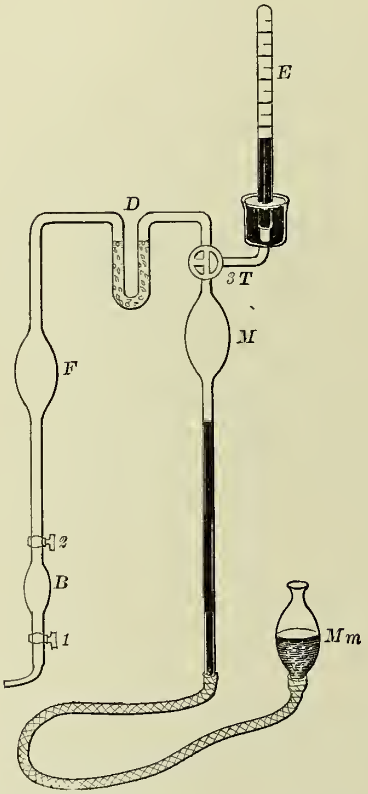
ANIMAL.	CONDITIONS.	R. Q. $= \frac{\text{Vol. } CO_2}{\text{Vol. } O_2}$
Ox.	On carbohydrate diet. (Herbivorous.)	1.00
Horse.	On carbohydrate diet. (Herbivorous.)	1.00
Sheep.	On carbohydrate diet. (Herbivorous.)	0.88
Rabbit.	On carbohydrate diet. (Herbivorous.)	0.90–1.00
Dog.	On mixed diet. (Omnivorous.)	.9
Calf.	On milk diet.	0.86
Man.	On carbohydrate diet. (Omnivorous.)	0.8–0.90
Dog.	On flesh diet. (Carnivorous.)	0.7
Cat.	On flesh and milk diet.	0.8
Rabbit.	Fasting.	0.7
Dog.	Fasting.	0.7
Marmot.	Awake.	0.8
Marmot.	Asleep. (Hibernating.)	0.5

b. Respiratory Changes in the Blood.

1. **The Gases of the Blood.**—One of the functions of the blood is to carry oxygen from the lungs to the tissue, and carbon dioxide from the tissue to the lungs. The next step in our inquiry is to subject arterial and venous blood to a vacuum to determine how much oxygen and CO_2 arterial and venous blood will yield under those conditions.

(*a*) THE METHOD OF EXTRACTING THE GASES OF THE BLOOD is shown in Fig. 145. When subjected to a vacuum the gases leave the blood, and after being freed from moisture they may be drawn first into the fixed mercury bulb (M), and then, through adjustment of the three-way tap ($3T$), sent into the eudiometer (E), where they are collected above mercury and may be subsequently analyzed.

FIG. 145.



Plan of apparatus for extracting the gases of the blood. To extract gases from the blood; 100 c.c. of blood is drawn in the blood-bulb B from the artery or vein. By closing tap 1 and opening tap 2, the blood is exposed to the conditions which exist in the rest of the apparatus. Suppose that the movable mercury bulb Mm had been previously held at the level of the fixed mercury bulb M; if it be lowered to the position shown in the figure there will be a rarefaction of the air in F, D, and M, and the gases will begin to escape from the blood. If a vacuum be previously established in the apparatus above tap 2, the turning of that tap will subject the blood to a vacuum, the gases will escape with such force as to fill the froth-chamber F with froth or bubbles from the blood; but the drying-tube D removes all moisture from the gases, which may be drawn through the three-way tap $3T$ into m by lowering Mm. If now, $3T$ be turned to the left 90° and Mm be raised the extracted gases will pass *Eudiometer* E where it is received above mercury and may be measured. A repetition of the process with a warming of the blood-bulb will enable the experimenter to extract all of the gases.

(b) THE RESULTS.—One hundred c.c. of blood, whether arterial or venous, yields about 60 c.c. of mixed gases. Pflüger found in the arterial blood of the dog 58.3 volumes per cent. of gases composed of oxygen, 22.2 per cent., CO_2 34.3 per cent., and nitrogen, 1.8 per cent. Zuntz found that venous blood contains 7.15 volumes per cent. less oxygen, and 8.2 per cent. more CO_2 than does arterial blood; nitrogen being the same in both.

2. **The Relations of Oxygen in the Blood.**—If the oxygen is in a state of simple solution in the blood as it is in the water—as described in the physical introduction—we shall expect it to give up its oxygen to a forming vacuum in proportion to the falling oxygen-pressure. Suppose we make the experiment. (See Fig. 146.) Let the line nO of the figure represent the gradual fall of oxygen pressure. If the line xO represents the quantity of oxygen dissolved in the blood, then according to the physical laws given above—the Henry-Dalton law of absorption of gases—the decrease in the quantity of dissolved oxygen would be represented also by a line nO; but the curve npO represents what actually takes place; *i. e.*, the oxygen is given off very slowly until the pressure is reduced to one-third or one-fourth and then it escapes very rapidly and not proportionally to the pressure.

On the other hand, if the oxygen-pressure is gradually increased, as in the line On', the quantity of that gas does not increase proportionately, but is represented by the curve $Op'n'$, *i. e.*, the oxygen is absorbed very rapidly at first and very slowly later. But we have ignored the fact that the blood is composite. Let us make the experiment with plasma, or better, with serum. We will release only a small quantity of oxygen by reducing the pressure to zero—a quantity represented by the line xP, and the line nP represents the gradual decrease with decreasing pressure. It appears then that the small quantity of oxygen which is associated with the plasma obeys the Henry-Dalton law, and must, therefore, be simply dissolved. If the red blood corpuscles, or better, if a strong solution of hæmoglobin, be subjected to the same experiment, we will find that at first no oxygen is given up, then suddenly all of it is given up rapidly with the falling pressure, but not proportionately to the pressure. (See curve HhO.) If the pressure be gradually increased the oxygen will be taken up very rapidly at first until the hæmoglobin is satisfied after which no more will be taken up. (See curve $Oh'H'$.) The quantity of oxygen absorbed by the hæmoglobin of a given quantity of blood may be represented by the line PO. From this we find: (I) the hæmoglobin takes up vastly more oxygen than does plasma; (II) the small amount of oxygen held by the plasma is in simple solution and obeys the Henry-Dalton law; (III) the oxygen which is held by the hæmoglobin is not dissolved; it is held by chemical affinity, the combination being called *oxyhæmoglobin* and written $Hb\text{-}O$; (IV) the oxygen can be separated from hæmoglobin only at low oxygen-pressure, and unites with hæmoglobin readily at much below atmospheric oxygen pressure.

Fig. 146.

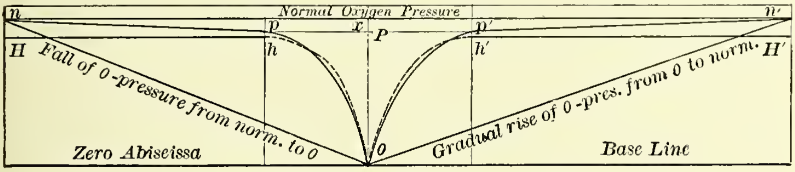


Diagram showing relation of oxygen in the blood.

3. **Relation of CO_2 in the Blood.**—We have found that less than three volumes per cent. of CO_2 represents the equilibrium of absorption of that gas in the lungs. From the physical laws above given we should expect the quantity of CO_2 in the blood to be small and the amount left in the blood after having passed the lungs, *i. e.*, the amount of CO_2 in arterial blood, to approximate the equilibrium, 3 volumes per cent.

The report of a series of experiments will aid us at this point of the discussion :

Experiment (*a*) If arterial blood be subjected to a zero CO_2 pressure it will give off 40 volumes per cent. of CO_2.

Experiment (*b*) If plasma be subjected to similar conditions it will give off 13 to 26 (average 20) volumes per cent. of CO_2.

(*c*) If venous blood be observed in the same way 45 to 46 volumes per cent. of CO_2 will be collected.

(*d*) The red-blood corpuscles alone yield under similar conditions about 15 volumes per cent. of CO_2 (5 per cent. to $7\frac{1}{2}$ per cent. of whole blood).

(*e*) Plasma plus weak acid will yield in *vacuo* about 30 volumes per cent. CO_2.

(*f*) Plasma plus Hb will yield in *vacuo* about 30 volumes per cent. CO_2.

These experiments and observations justify the following conclusions :

(*a'*) More CO_2 is contained in the blood than can be accounted for on the basis of physical laws.

(*b'*) The plasma contains about two-thirds of the CO_2 and it is, for the most part, in chemical combination.

(*c'*) The CO_2 of the plasma must in part be held in weak chemical combination and in part in strong chemical combination ; because a part of the chemically combined CO_2 is released at zero CO_2 pressure. At this point it is neeessary to inquire : (I) In what chemical combinations does CO_2 exist in the plasma? (II) Is one of these affected by CO_2 pressure ? Carbon dioxide exists in the plasma in combination with sodium as $NaHCO_3$ and Na_2CO_3. Of these two compounds the former is a weak one and at zero CO_2 pressure will part with that gas according to the following equation :

$$2NaHCO_3 = Na_2CO_3 + H_2O + CO_2.$$

Now, the addition of a weak acid, or of HbO, further decomposes the Na_2CO_3, thus liberating the last of the CO_2. The Na_2O probably joining to $2NaH_2PO_4$ to make $2Na_2HPO_4 + H_2O$.

(*d'*) About one-third of the CO_2 of the blood is held by the red-blood corpuscles. It is supposed that this is for the most part held in a loose chemical combination with the hæmoglobin of the corpuscles, in fact with the globulin component of the hæmoglobin.

(*e'*) Hæmoglobin, especially oxy-hæmoglobin, acts as an acid, and the more stable carbonates of the blood are broken up in the presence of HbO and *a zero CO_2 pressure.*

Our next task is to weave these facts and conclusions into a consistent theory. Preliminary to this let us define the word *tension* as used by the physiologist in this connection. If the partial pressure of a gas be increased or decreased the quantity absorbed will rise or fall accordingly. It is evident that the gas must be under a certain degree of pressure to prevent its passing out of solution. The gas in solution is said to be under *tension.* "If the partial pressure of this gas (in the air) diminishes, the gas in solution is given off until the partial pressure of the gas in the air and the tension of the gas in solution are equal." *Tension* is expressed in the same terms as *pressure, i. e.,* in mm. of mercury. The tension of CO_2 in the tissues = 7.66 per cent. of 760 mm. = 58.25 mm. In the venous blood = 41.4; in arterial blood = 21.28; while the partial pressure of this gas in the alveoli equals 5 per cent. of 760 mm. of mercury equal to 38 mm. of mercury. Inasmuch as the $NaHCO_3$ of the plasma will tend to change to a more stable compound, giving up one-half of the CO_2 in the lower CO_2 tension of the lungs, we shall expect to find the CO_2 passing regularly from a place of high tension to one of low tension. It will naturally then diffuse rapidly from the tissues with their tension of 58 + to the blood, which enters the capillaries of the tissues with a tension of 21 +, and leaves the capillaries *en route* for the lungs with a CO_2-tension of 41 +, nearly double what it entered the tissues with, but still considerably below tissue tension (58). It must be stated at this point that the diffusion is made possible by two things working together, both tending to take up simply dissolved CO_2 from the plasma, store it away, so to speak, in a chemical combination. (I) The hæmoglobin, which just parted with its oxygen, may now satisfy its affinities with CO_2, which it does, thus making place for more CO_2 to diffuse into the plasma. (II) CO_2 has a strong affinity for sodium. This element does not exist free or in loose combination, except with Na_2HPO_4. So that the phosphoric acid is forced to part with its second atom of sodium, as shown in the following equation:

$$Na_2HPO_4 + CO_2 + H_2O = NaH_2PO_4 + NaHCO_3$$

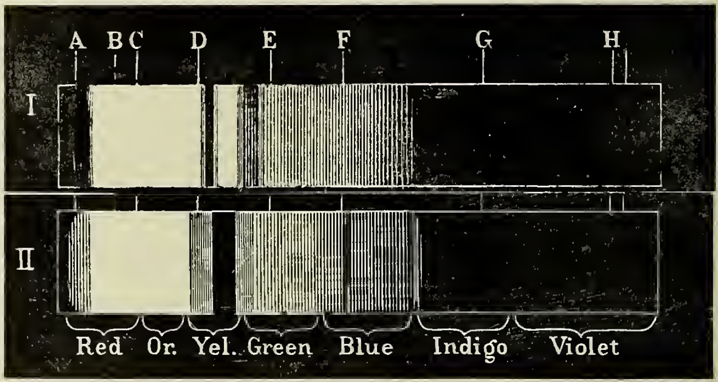
The venous blood passes to the lungs, having received an increase in CO_2 which has been largely taken into such chemical combinations as $NaHCO_3$. Leaving the amount dissolved in the plasma varying little probably from that which is found in the arterial blood. Reaching the lung capillaries the conditions are reversed. The high oxygen tension (122) of the alveoli favors the reversal of the reaction between the hæmoglobin and the oxygen and carbon dioxide gas. The stronger affinity of hæmoglobin for oxygen causes it to drop the CO_2 and take up oxygen forming Hb-O, the CO_2 is first taken up by the plasma thus further increasing the CO_2-tension in that liquid and further hastening diffusion toward the alveoli. Besides this interchange we must not forget that the low

CO_2-tension in the lungs favors the reversal of the reaction between NaH_2PO_4 and the $NaHCO_3$ so that we have the following reaction :

$$NaH_2PO + NaHCO_3 = Na_2HPO + H_2O + CO_2$$

Just how far this reaction between phosphoric acid and carbonic acid plays a part in actual respiration is still undetermined. Equally undetermined is the importance of the relation between Hb and CO_2. That the reactions take place when plasma or a solution of these compounds is under experimental test is demonstrated. But we must remember that we have only to account for an addition of six volumes per cent. of CO_2 in the tissues and a release of the same amount in the lungs and it is not certain that the reaction in question plays any important part in it. It may be that the transfer of CO_2 is accomplished solely through the laws of diffusion without the intervention of chemical reactions.

FIG. 147.



I, spectrum of oxyhæmoglobin ; II, spectrum of reduced hæmoglobin. (After DALTON.)

4. **The Influence of Blood-gases upon the Spectrum.**—In any spectroscopic examination of the blood account must be taken of the fact that hæmoglobin reacts very differently under different conditions : (I) When combined with oxygen as oxyhæmoglobin (Hb-O) it shows two absorption bands as shown in Fig. 147, I ; (II) when it is deprived of its oxygen, *i. e.*, reduced to hæmoglobin the light absorption takes place in one broad band which nearly corresponds to the two above with the space between them. (See Fig. 147, II.)

2. INTERNAL OR TISSUE RESPIRATION.

The terms external and internal respiration are used to designate different phases of the same general process. The essential process is the providing of oxygen to the active cells, where it is combined with the cell plasma either in some of the steps of anabolism or in some of the earlier katabolic steps. This ultimate step of respiration is called "*tissue respiration,*" or "*internal respiration.*" A still better term would be *cell respiration*. Cell respiration then consists in taking up of oxygen from the intercellular plasma and utilizing it in metabolic,—usually katabolic,—processes. The ultimate products of katabolism are CO_2, H_2O, etc. These end products are useless to the cell and are ejected into intercellular plasma. It is evident from this that cell-respiration is simply one phase of cell nutrition which deals with the gaseous elements of assimilation (oxygen) or of excretion (CO_2). The term external respiration is applied to all those processes by which air is introduced into the lungs, the oxygen taken up by the blood, the CO_2, given off by the blood and the transfer made with the tissue plasma. The relations between external respiration and internal or cell respiration may best be illustrated by a diagrammatic scheme of the respiration. The oxygen of the atmosphere enters the zone of tidal air where the oxygen pressure may be represented by O, from this zone it rapidly diffuses with the zone of reserve air where the oxygen pressure is lower and may be represented by O'. Thence it diffuses into smaller bronchioles and alveoli where the pressure is still lower and may be represented by O''. The lower pressure (O''') of the capillaries invites it to pass through the two delicate membranes which separate it from the lumen of the capillary. Once in the blood current it is swept along as Hb-O to the active cells where the oxygen pressure is practically zero (O''''). Here the hæmoglobin gives up its oxygen, or the oxygen is dissociated, is dissolved in the cell plasma in part or passes directly into the living cells where it is at once chemically combined in the cell metabolism. But the blood, now robbed of oxygen, is in the presence of very

FIG. 148.

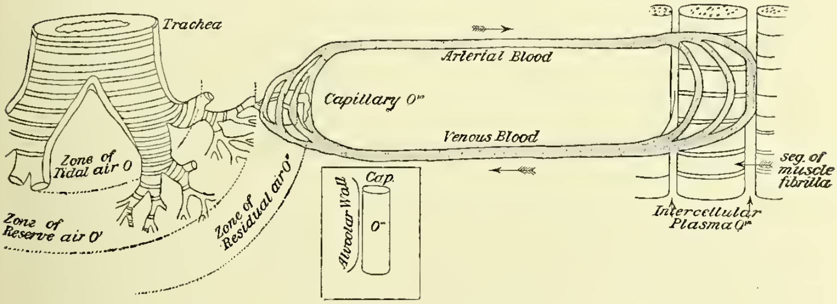


Diagram showing relation between external and internal respiration.

high CO_2 pressure, the hæmoglobin is instrumental in holding chemically a certain amount,—let us say provisionally, as Hb-CO_2,—the rest is taken up in simple solution in the plasma. Thus laden the blood is brought back to the air cells of the lung where the hæmoglobin at once releases the CO_2 and takes up oxygen, forming again Hb-O. The CO_2 after its release from the corpuscles is in the plasma from which it rapidly diffuses into the alveoli, because of the low CO_2-pressure there. The relations may also be expressed thus: O-pressure in tidal air (158 mm.) $>$ O-pressure in reserve air $>$ O-pressure in residual air (122 mm.) $>$ O-pressure in capillary (30 mm.) $>$ O-pressure in tissues. CO_2-pressure in tidal air 0.3 mm. $<$ CO_2-pressure in reserve air $<$ CO_2-pressure in residual air (38 mm.) $<$ CO_2-pressure in capillary (41 mm.) $<$ CO_2-pressure in tissues (58.25 mm.).

Richert (American Text-book of Physiology, p. 526) uses the following very effective method to show why the O passes from the alveoli of the lungs into the blood and CO_2 in the reverse direction:

	O	CO_2
Tension in alveolar air	122	38
Pulmonary membrane	↓	↑
Tension in venous blood	22 +	41 +

In a similar way he shows graphically why the diffusion currents are reversed in the tissues:

	O	CO_2
Tensions in arterial blood	29.64	21.28
Blood vessel walls	↓	↑
Tensions in tissues	0.0	58.25

Having defined the external and the internal respiration and having shown the forces which operate in the movements of the gases of respiration it remains to treat briefly the relation of cell respiration to general cell metabolism. This has been done in some detail under General Physiology so that a brief summary is all that is here required.

Summary of the Principles of Cell Respiration.

(1) The increase of the supply of oxygen does not increase the activity of the cell or tissue.

(2) The increase of cell activity is accompanied by an increase of need for oxygen followed by an increase of the supply of oxygen.

(3) The amount of CO_2 given off by the cell is proportional to its activity; and is, therefore, *a measure of cell activity.*

(4) Cell activity takes the form of *liberation of energy.* This

energy is the potential energy of cell protoplasm (or energy-producing material held by the protoplasm—see metabolism) and is liberated not by direct oxidation, as in combustion; but by indirect oxidation.

(*a*) "By integration of O a force-yielding storage-substance is formed" (Waller).

(*b*) By disintegration of this substance carbon dioxide is liberated in company with other material katabolites and energy in the form of heat, work, and electricity.

C. THE CONTROL OF THE RESPIRATION.

1. INNERVATION OF THE RESPIRATORY ORGANS.

a. General Experiments and Conclusions.

A dissection of the respiratory system would reveal the presence of the intercostal nerves, one just posterior to each rib, giving off fine branches to the intercostal muscles; followed toward the central nervous system, these nerve trunks are found to emerge from the spinal cord by two roots, an anterior nerve-root and a posterior nerve-root. One would find the diaphragm supplied by a pair of large nerves which may be traced up through the mediastinum out of the thorax, into the deep muscles of the neck where they are found to be a part of the cervical plexus and to arise from the III, IV and V cervical nerve-roots; these are the phrenic nerves. Further, we remember that the vagus gave off, besides the cardiac branches, the superior laryngeal and inferior laryngeal and the remaining trunk is largely distributed to the tissue of the lungs, though a part of the trunk extends as far as the stomach. If we follow the distribution of the vagus in the lungs we will find that its branches enter the root of each lobe and are distributed along the air passages supplying the mucous membrane and the involuntary muscles of the bronchioles. Physiological experiment alone can determine the action of these different nerves.

1. **Experiments.**—(I) Cut one or more of those lower intercostal nerves which supply the abdominal muscles; the muscles will cease to act in expiration.

(II) Cut one or more of those upper intercostal nerves which supply the external and internal intercostal muscles; the muscles in question cease to act, *i. e.*, the external intercostals cease to elevate the ribs in inspiration and the internal intercostals cease to depress the ribs in expiration.

(III) Cut the posterior nerve-roots of any of the intercostal nerves; the results above observed in cutting the whole nerve trunk are noted in this case.

(IV) Cut the anterior nerve roots of any of the nerves in question; the result is the same as if the whole trunk were severed.

(V) Cut the phrenic nerves; the diaphragm ceases its movements.

(VI) Cut the vagi; inspiration is deeper and the respiratory movements slower.

(VII) Cut the superior laryngeal; a tickling of the larynx will not cause coughing—expiration.

(VIII) Cut the inferior laryngeal or recurrent laryngeal; all contractions of glottis and tracheal muscles cease.

(IX) Cut the spinal cord just above the first intercostal; all respiratory movements of the ribs and of the abdominal muscles cease.

(X) Cut the spinal cord just posterior to the medulla oblongata; all respiratory movements of the ribs, diaphragm and abdominal muscles cease, but the glottis, larynx and nostrils will make spasmodic efforts at inspiration.

(XI) Cut or sever brain from medulla—everything else being intact, the rhythm and depth of the respiratory movements are not disturbed. Excite the animal; no change in depth or rhythm.

2. **Conclusions** from these experiments in order:

(I) The lower intercostal nerves carry motor fibers of both inspiration and expiration.

(II) The upper intercostal nerves carry motor fibers of both inspiration and expiration.

(III, IV) The motor fibers pass out of the spinal cord via the anterior nerve roots.

(V) The phrenic nerve is the motor nerve of the diaphragm, and, therefore, a motor nerve of inspiration.

Any of these conclusions may be verified by stimulating the distal end of any of the cut nerves; in every case the muscles supplied will contract, showing the nerves to be, in part at least, afferent motor nerves.

(VI) From experiment (VI) it is difficult to say exactly what the function of the vagus is. Inasmuch as the nerve is supplied largely to mucous membranes, we cannot expect it to be motor in its action. Suppose the distal end be stimulated; no very noticeable change takes place. Now stimulate the central end; respiratory movements are at once affected. A carefully adjusted stimulus of the central ends may lead to normal respiratory movements. A strong stimulation to the central end of the vagus will lead to a more rapid rate of respiratory movements and a final standstill of the diaphragm either at the end of expiration or inspiration, *i. e.*, diaphragm either in tetanus or in paralysis. These results prove the vagus to carry *afferent* or *sensory* fibers, and the ambiguous results may be accounted for as the result of *two kinds of sensory fibers*, one kind stimulating the inspiratory center and another kind stimulating the expiratory center.

(VII) The superior laryngeal is a sensory nerve stimulating explosive expiratory acts.

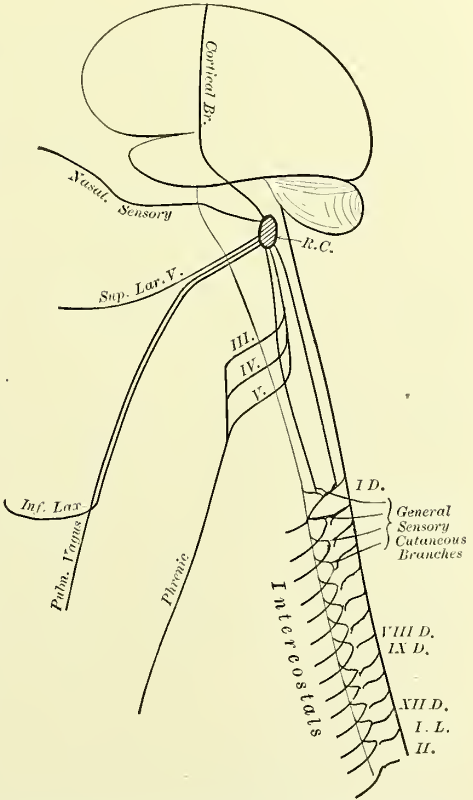
(VIII) The recurrent laryngeal is the motor nerve of the glottis, laryngeal and trachea. Stimulation of the distal end confirms the conclusions, for the muscles of this region contract vigorously.

(IX) The respiratory center for intercostals and abdominal muscles is above the dorsal cord.

(X) The general respiratory center is not posterior to the medulla.

(XI) The general respiratory center is not anterior to the medulla. The *center is located in the medulla*, in the floor of the fourth ventricle, just posterior to the cardio-inhibitory center. It is found to be symmetrically located in the two lateral halves, though these communicate and act in harmony they may be separated and still act synchronously, but may be made to act inharmoniously by special stimulation of one-half. Each half is further believed to consist of an inspiratory and of an expiratory nucleus. From experiments (X) and (XI) it is clear that the *center is automatic*. From experiments (VI) and (VII) it is shown that the *center is also reflex*.

FIG. 149.



Schema of innervation of respiratory organs; *R.C.*—Respiratory center in the spinal cord. *V*, vagus with superior laryngeal, inferior laryngeal and pulmonary branches. Phrenic supplying the diaphragm; intercostals supplying the inspiratory and expiratory muscles of the thorax and the expiratory muscles of the abdomen. All cutaneous sensory nerves affect the respiratory center. Nasal sensory may precipitate sneezing or otherwise affect respiration.

b. The Action of the Respiratory Center.

1. **Through its Automatic Action** the center would send intermittent *spasmodic inspiratory* or *expiratory* impulses along the efferent nerves to the respiratory muscles. The automatic action

of the respiratory system is analogous to that of the circulatory system.

2. *Reflex influence from the Periphery* is an important factor in the control of the rhythm and depth of the respiratory movements. There are two ways in which this is accomplished viz., directly and indirectly.

(*a*) DIRECT REFLEX STIMULATION may in turn be accomplished: (I) *through the influence of the blood supply;* (II) *through the influence of sensory impulses.* (*α*) *The influence of the blood supply.* In this connection we remember that the cardiac center in the medulla is affected by the quantity and quality of the blood which it receives from the heart through the carotid and vertebral arteries. In the same way the respiratory center is affected by blood from the same source. In this case the quality of the blood is of more importance than the quantity, *i. e.*, it is the quantity of oxygen and of carbon dioxide which stimulates the center. Each inspiratory act is precipitated by the stimulating presence of an excess of CO_2 in the respiratory center, while the expiratory acts are less affected by the CO_2 of the blood until this accumulates to an abnormal degree; even then it may be rather lack of oxygen than excess of CO_2, which causes the change in respiratory movements. Fredrick performed a most interesting experiment with two dogs. The vertebral arteries were ligated; the carotids of dog A were joined through cannulæ to the distal ends of those of dog B and those of dog B connected with those of dog A, so that the blood of dog A circulated in the head of dog B and *vice versa.* The experiment consisted in suddenly closing the trachea of dog A; after a few moments dog B began to gasp for breath. The reason is clear: the excess of CO_2 from the circulation of dog A stimulated the respiratory center of dog B, leading to his much increased respiratory movements.

(*β*) *Under the influence of the sensory impulse* we may first enumerate those which come from the vagus. When the lungs become distended to a certain degree the sensory fibers of the vagus send an impulse to the center which precipitates an expiration. Again, an impulse from the superior laryngeal may cause a spasmodic contraction of the abdominal muscles, causing a cough. Certain irritating gases—Cl, SO_3, etc., affect the sensory nerves of the nose and larynx, and cause the center to block all respiration. Such gases are called irrespirable.

(*b*) INDIRECT REFLEX STIMULATION of the respiratory mechanism may be correctly so distinguished because the respiratory acts are induced or influenced by impulses from nerves only indirectly connected with the respiratory mechanism. A sudden dash of cold water will cause an inspiration. When a child is being delivered feet first at birth care must be taken that the delivery be made rapidly, or that the body be protected from drafts of air, for the stimulation by the air may cause inspiration and the child may draw the respiratory passages full of mucus, which will greatly complicate the induction of normal respiration.

3. **Cerebral or Voluntary Influence on the Respiration.**—Besides the automatic action and the reflex influence of the center, there is a marked influence from the cerebrum. In fact, if one gives his attention to it he may govern his respiratory movements as to rhythm and depth up to a certain point. Certain states of mind may modify respiration—coughing, crying, sighing, etc. One cannot, however, stop respiration voluntarily long enough to take his life. The accumulated impulses finally become too strong to control by the mind and the diaphragm descends.

c. Unusual Respiratory Conditions.

In contradistinction to the usual and normal respiration, which is called EUPNŒA, there are several conditions which deserve mention.

1. **Apnœa.**—Complete cessation of respiration. One can "hold his breath" much longer if he precedes his efforts by a series of rapid, deep breaths. If the air be vigorously and rapidly forced into the lungs of an animal by artificial respiration for a minute, some time will elapse before the animal evinces any tendency to breathe. The most natural inference—that he has O enough to last a minute or two—is not the correct inference, for experiment has shown that the blood may accumulate a marked excess of CO_2 before the center is able to overcome inhibition, which it is receiving from some source. And what source? From the over-stimulated sensory ends of the vagus.

2. **Hyperpnœa.**—Usually deep breathing, such as one is led to from too strenuous muscular exertion.

3. **Dyspnœa.**—Painful breathing. All conditions which diminish the O or increase the CO_2 in the blood circulating through the medulla, if carried beyond a certain point, produce a labored respiration which can no longer be recognized as hyperpnœa. All the phenomena of extreme forced respiration, together with signs of the greatest discomfort, or even pain, make up the symptom-complex of dyspnœa. It is not an infrequent symptom of disease, and may occur under the following conditions:

(*a*) *Direct limitation* of the *activity* of the *respiratory organs:*

(I) *Diminution* of *respiratory* surface, as in pneumonia, or acute œdema of lungs. (II) *Entrance* of air or fluid into *pleural cavities*—pneumothorax and hydrothorax. (III) Obstruction of trachea or larynx; croup, etc., strangulation. (IV) Contraction of bronchioles—asthma.

(β) *Enfeeblement of circulation.* (I) In degeneration of heart muscle. (II) Valvular disease of heart.

4. **Asphyxia.**—This term is used to express the condition of collapse after a failure of the system to get O or to eliminate CO_2. Such a condition is always preceded by (I) *Hyperpnœa;* (II) *Dyspnœa,* and (III) *Convulsions.* Death by asphyxia occurs in four stages, the three just noted, followed by *collapse* and *death.* The term is used to indicate death by drowning, by suffocation, by strangulation, etc.

CHAPTER V.

DIGESTION.

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3. THE EVOLUTION OF SALIVARY GLANDS.
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DIGESTION. INTRODUCTION.

A. THE COMPARATIVE PHYSIOLOGY OF DIGESTION.

1. INTRACELLULAR DIGESTION.

In the nature of the case an organism which consists of only one cell must take in nutriment through the ectosarc or exoplasm into the endosarc or endoplasm of the cell. If the nutriment be fluid the absorption is a simple process, influenced largely by the physical laws of osmosis, and may be followed by a rapid assimilation of the absorbed nutriment. If the nutriment be solid the process of taking it through the ectosarc is a mechanical one and is accomplished by movements of the protoplasm. Once the solid particle of food is engulfed in the endosarc a true process of digestion or solution is necessary before the nutriment may be assimilated or built up into cell protoplasm. For a concrete description of the whole process of nutrition, including digestion, in the unicellular animals, particularly the amœba, the reader is referred to *General Physiology* (p. 42). The digestion in unicellular animals is necessarily of the intracellular type. *The Cœlenterates* afford an example of a type of animal in which a definite tissue is set apart for the function of digestion. This specialized tissue, the entoderm, lines a cavity or a more or less complex series of cavities formed by an invagination or dipping in of the surface of the developing organism. Solid nutriment taken into these cavities is taken up by the endodermal cells which line the cavity, and digested within them. The product of digestion is in part passed on to the non-digesting tissues by diffusion or by circulation through the *gastrovascular canals*. Among the cœlenterates at least one form has been discovered—"the fresh water medusa—in which, the cells which line the mouth of the gastric tube have the function of secreting a digestive fluid" (Lankester). But this cœlenterate retains the primitive intracellular method of digestion throughout the greater part of the gastric tube.

2. DIGESTION BY SECRETED FERMENTS.

The transition from the primitive to the higher mode of digestion is a gradual one. The lowest worms—Turbellaria—have the intracellular mode, and the mesoblastic cells of echinoderm larvæ manifest the same property. In this connection one recalls also the intracellular digestion of bacteria, etc., by the leucocytes of the higher animals.

All higher invertebrates and vertebrates possess an alimentary canal through which the food passes while being acted upon by various ferments which produce a progressive series of digestive changes. This canal is usually differentiated into several distinct divisions in which particular steps of the process are performed. In the early part of the process the food is triturated. Either before, during or after trituration it is softened and lubricated by secretion of the alimentary canal. The food is passed along the canal by a peristaltic motion of involuntary muscles within the wall of the canal. Dissolved (digested) portions of the food are removed by absorption through the wall of the alimentary canal. The absorption surface is much increased (I) by the coiling of the digestive tube, (II) by the folds of the lining of the tube, and (III) by finger-like projections on the surface of the folds, the last method for the increase of surface being especially pronounced in the higher vertebrates.

3. THE EVOLUTION OF SALIVARY GLANDS.

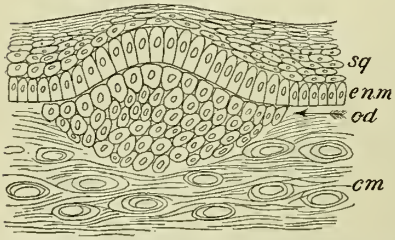
The walls of the oral cavity are provided with mucous glands which are all developed by invagination of the epiblastic epithelium of that cavity and have the form of simple or compound tubular glands. In the lower vertebrates there is no very marked difference in the structure or function of the glands in the different regions of the oral cavity, except that those of the tongue are, perhaps, somewhat more highly developed and more active than those of the palate, cheeks or sublingual region. Among the higher amphibia, where the tongue is so often used as an organ of prehension, the lingual glands are highly developed and their secretion is driven out upon the surface of the tongue with every contraction of that organ. The aquatic reptiles have illy developed oral glands, while the terrestrial reptiles, like the terrestrial amphibians, have well developed lingual glands, as well as submaxillary glands, the latter secreting in some lizards a poisonous mucus. In birds the lingual, and in many cases the sublingual, glands are well developed, while the labial, buccal and submaxillary are naturally absent. In the mammals three pairs of large, ordinarily acinous, glands predominate over the smaller and more scattered buccal glands. These, from their positions, are distinguished as the PAROTID, SUBMAXILLARY and SUBLINGUAL glands. "From our knowledge of the influence which the secretion of these glands has on the starchy foods in ourselves, it is often thought that therein lies their primary function. Certain considerations seem to show that this is not a correct view. In the Cetacea and other aquatic mammals, and in the blood-sucking Desmodus, the glands are small, while the kangaroo, which dwells in the arid plains of Australia, has the glands in question of great size. It would seem that the prime function of these structures is to afford a supply of water for the solid food. A physiological advantage is gained by the fact that this water has the temperature of the body." (Jeffrey Bell.)

"The well-known fact in human physiology that the secretion of the parotids is more watery and that of the submaxillary and sublinguals more viscid, is paralleled in comparative anatomy by the large size of the parotids in animals which masticate dry foods, as do the Herbivora, and by the great size of the submaxillary in such animals as the ant-eater, which requires a viscid fluid for the purpose of catching its prey." (W. A. Forbes.)

4. THE EVOLUTION OF ORAL TEETH.

Among the lower vertebrates one finds teeth located in the oral cavity and the inner surface of the branchial arches in immense numbers,—as palatal, lingual, and pharyngeal teeth,—but they are also distributed in close-set rows over the whole surface of the skin, and produce, as in the sharks, a strong but flexible coat-of-mail. (Hertwig.)

Fig. 150.

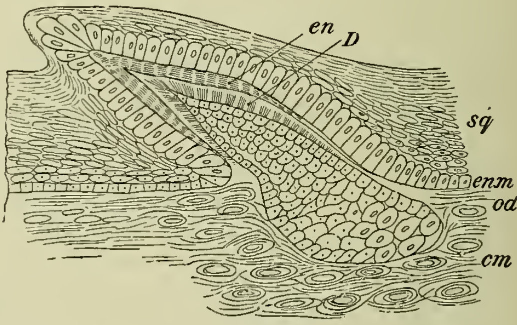


First stage of development of a shark's dermal tooth. *enm*, enamel membrane from epiblast; *od*, odontoblast layer from mesenchyme; *cm*, cementum fundament; *sq*, squamous epiblast.

The reader remembers that the oral mucous membrane is derived from the invaginated epiblast; that, in common with the skin, it presents mesenchymal papillæ; and that these papillæ obey the general biological law of the *physiological division* of *labor* accompanied by *differentiation* of *structure.*

With these facts and considerations in view let us study the development of a shark's dermal tooth. (See Figs. 150 and 151.)

Fig. 151.

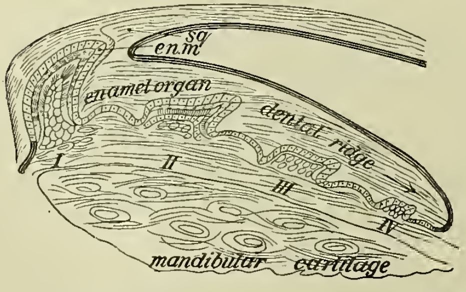


Second stage of a shark's dermal tooth. *en*, enamel; *D*, dentine.

Compare it with that of the shark's oral tooth (see Fig. 152); also with that of a higher vertebrate.

From these figures it is evident: (I) That the dermal and oral teeth of the shark are practically identical in development and structure; and (II) that both are modified mesenchymal papillæ. The epithelial tract of the oral mucous membrane which shares in the formation of the teeth has sunk deep down in the form of a ridge on the inner surface of the mandibular arch, and into the loose connective tissue. It now represents a special organ,—the *enamel organ* or dental organ. In sharks and in lower vertebrates generally the replacement of old teeth by

Fig. 152.



Dental ridge and enamel organ of a shark's oral tooth. *I–IV*, successive generations of teeth. (After Hertwig.)

new ones is an unlimited process (see Fig. 152, *I–IV*); but as the rank becomes higher the process is more limited, and in mammals the replacement occurs only once;—*i. e.*, the "*milk teeth*" are replaced by the *permanent teeth*. One finds, therefore, in mammals that the *dental organ* or *enamel organ* has only two papillæ, one of them giving rise to a temporary tooth and one to a permanent tooth.

In all of those lower vertebrates provided with oral teeth those organs are used as instruments of prehension or of defense or offense. Even in the highest vertebrates the teeth retain the primitive function to a limited extent. In the higher mammalia another function becomes prominent, viz., that of grinding the food. This function is most highly developed in the herbivora and omnivora, in which divisions of mammals the teeth are strongly modified structurally to adapt them to this end. Among the carnivora the primitive functions predominate and the teeth are correspondingly modified to adapt them for the most efficient prehension, and offense and defense.

In primitive man the teeth are typical of the omnivora. In highly civilized man the teeth are, with each succeeding century, becoming weaker. They develop more variably, erupt more irregularly in time and place, and they decay earlier. All of these facts are indications of degeneration, and point toward an ultimately toothless human race.

B. ANATOMICAL INTRODUCTION.

1. A SUMMARY OF THE ANATOMY OF THE DIGESTIVE SYSTEM.

a. The System in General.

(*a*) THE DIGESTIVE SYSTEM consists of the *alimentary canal* together with certain *glands* whose ducts open into the canal.

(*b*) THE ALIMENTARY CANAL begins with the mouth and ends with the anus. It consists of: (*a*) The oral cavity; (*b*) the pharyngeal cavity; (*c*) œsophagus; (*d*) stomach; (*e*) small intestine, composed of duodenum, jejunum, and ileum; (*f*) large intestine, composed of cæcum, colon, and rectum.

(*c*) THE TUBE is lined throughout with mucous membrane, outside of which is a submucous coat. Both of these coats vary much in different portions of the tube. The mucous epithelium of the mouth and œsophagus is stratified while that of the stomach and intestines is columnar. The glands of the mucosa are variously modified in different parts of the anal. The submucosa is thin in the mouth and pharynx, but abundant in all other parts of the tracts.

(*d*) The Wall of the Free Tube—from the beginning of the œsophagus to the anus—contains muscular coats, covered externally with a fibrous coat. All of that portion of the canal within the abdominal cavity receives an outer peritoneal investment.

Fig. 153.

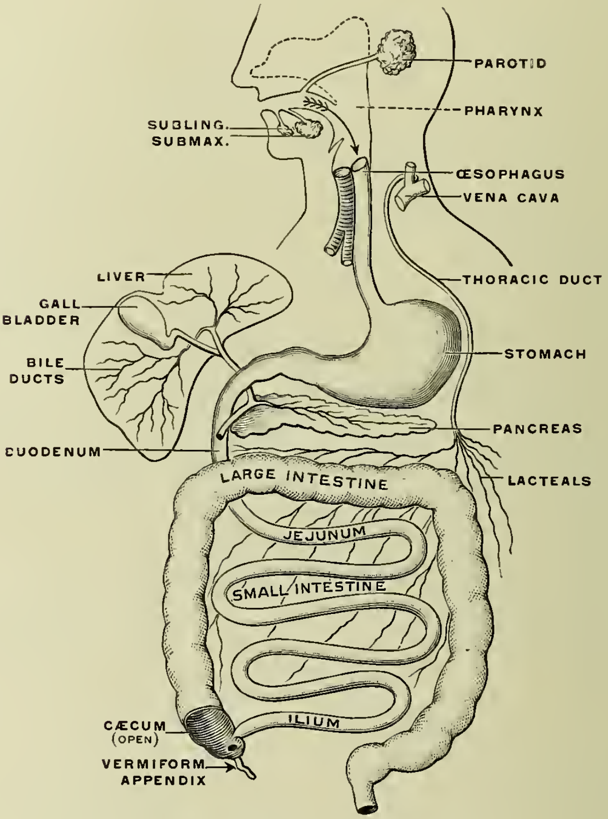


Diagram of the digestive tract. (After Landois.)

(*e*) A Typical Portion of the wall of the alimentary canal consists of: (I) *Mucous membrane*, whose epithelium is the *secreting* and *absorbing* portion of the wall; (II) *Submucous coat*, whose loose fibrous structure permits free folding and free movement of the mucosa, and furnishes a favorable course for blood vessels, lymphatics and nerves; (III) *Muscular coat*, whose two or three layers of involuntary muscle tissue perform the slow peristaltic contractions which are so important a factor in digestion; (IV) *Fibrous coat*, which lends additional strength to the walls of the tube. Usually included with this coat is the pavement epithelium of the peritoneum.

(*f*) THE EPITHELIUM OF THE MUCOUS MEMBRANE is hypoblastic in origin except in the mouth, upper pharynx and lower rectum. The serous epithelium of the peritoneal covering of the tube is from the *splanchnopleuric mesoblast.* All of the structures between these two epithelial boundaries (nerve-tissue excepted) represent *mesenchymic mesoblast.* The nerves invade these tissues from the "*neuroblastic*" *epiblast.*

(*g*) UPON THE INNER SURFACE of the mucous lining, innumerable glands open. These glands are developed in the embryo by evagination from the mucous surface; the gland epithelium has, therefore, the same histogenesis as the mucous epithelium from which it evaginated; the epithelium of all glands opening into the mouth being epiblastic, and that of all glands opening in the stomach, for example, being hypoblastic.

(*h*) A LARGE PROPORTION OF THESE GLANDS are mucous secreting glands. In certain locations the glands present both structural and functional modifications; in the stomach the peptic glands present structurally the striking parietal or acid cells while, functionally, these glands secrete both pepsin and hydrochloric acid.

(*j*) BESIDES THESE GLANDS WITHIN THE WALL of the canal there are several large glands,—salivary glands and pancreas,—which lie quite outside that wall of the canal and pour their secretion into the canal through a duct whose epithelial lining is continuous with the epithelium of the canal. The active cells of these glands are modified epithelial cells, and, with the lining of the duct are derived, in the embryo, by evagination from the lining of the alimentary canal.

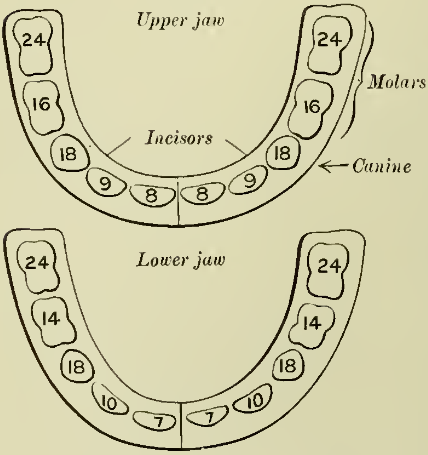
b. Particular Segments of the Tract.

1. **The Oral Cavity.**—This portion of the alimentary canal is especially adapted, by its firm stratified epithelium, to receive solid food. The skeletal and muscular structures which surround this cavity perform important parts in its functions. The skeletal portion of the roof of the cavity is formed by the superior maxillary bone presenting the palatal plate and the alveolar ridge, while the skeletal portion of the floor of the cavity is formed by the inferior maxillary bone presenting an alveolar ridge. These alveolar ridges are armed with teeth which are set in bony sockets lined with periosteum.

(*a*) THE TEETH.—For a description of the minute structure of the teeth the reader is referred to any work on histology. There are two sets of teeth, a *temporary* set and a *permanent* set. The time of eruption is important to the physiologist, because it is indicative of the kind of food which the organism requires. The time of *Eruption* of the *Teeth* is shown in Figs. 154 and 155.

(*b*) THE MUSCLES OF MASTICATION are those which produce the movements of the inferior maxillary bone, especially the temporales, the masseter, the pterygoid, also those which produce movements of the cheeks and tongue.

FIG. 154.



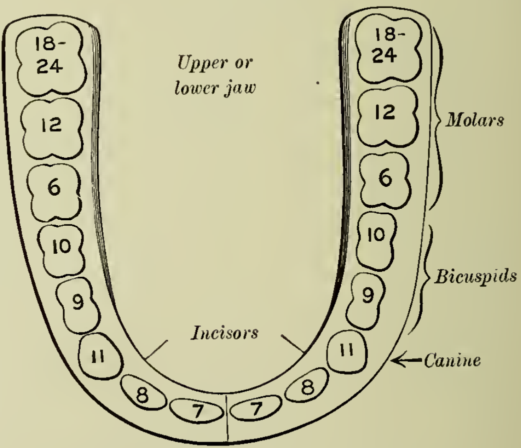
Temporary teeth. (Time given in months.)

(*c*) THE GLANDS OF THE MOUTH are the numerous mucous glands whose function is to keep the mouth moist, also the highly developed *salivary glands.* There are three pairs of salivary glands, the submaxillary, the sublingual and the parotid. (For Figures see Secretion.)

(*d*) THE TONGUE lies in the floor of the mouth, and is composed mainly of longitudinal and transverse muscle fibers, through whose combined action the tongue may be retracted, protruded, raised, lowered, or circumducted.

This organ is most useful in *mastication.* In some animals it is used as an organ of *prehension.* In most animals it is used as a *tactile* organ. In the mucous membrane of the tongue are located the principal end-organs of the *sense* of *taste.* Especially adapting the surface of the tongue for these various functions are the papillæ which are of three varieties : (I) the circumvallate, (II) the fungi-form, and (III) the conical. The first two forms named contain taste buds. (See Fig. 156.) (For other figures see Taste.)

FIG. 155.

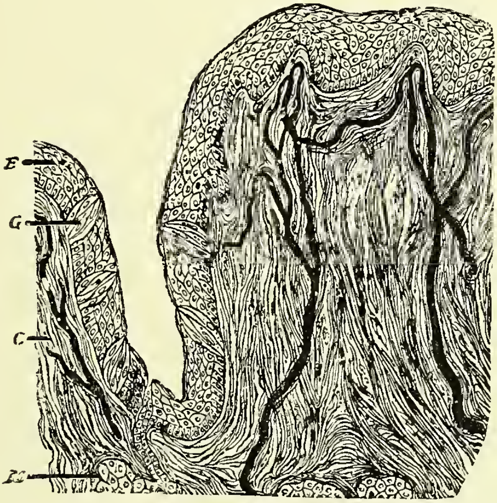


Permanent teeth. (Time given in years.)

2. **The Pharynx.**—The uvula marks the boundary between the oral cavity and the pharynx. This cavity is common to the digestive and respiratory systems. The portion of it which is concerned in swallowing is lined with stratified epithelium and is

supplied with mucous glands. Its walls contain three sets of muscles (*Pharyngeal constrictors*) whose contraction aids in deglutition.

FIG. 156.



Section of circumvallate papilla, human. The figure includes one side of the papilla and the adjoining part of the vallum. (Magnified 150 diameters.) (HEITZMANN.) *E*, epithelium; *G*, taste-bud; *C*, corium with injected blood vessels; *M*, gland with duct. (SCHAEFER.)

3. **The Œsophagus.**—This is the tube which leads from the pharynx, through the thorax to the stomach. It possesses the four typical coats described above. The mucous membrane presents longitudinal folds, and its epithelium is stratified. The numerous mucous glands dip down into the submucosa. The two heavy muscular coats serve the function of deglutition.

FIG. 157.

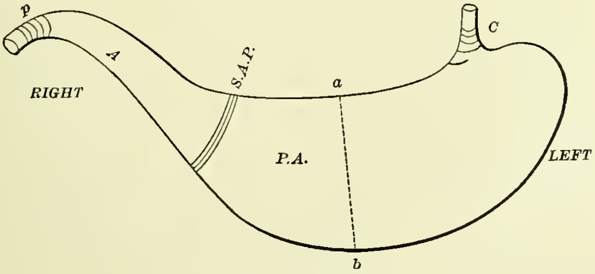
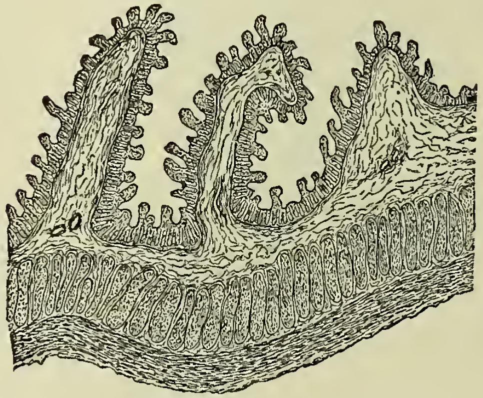


Diagram of the stomach.

4. **The Stomach.**—This very important viscus is a dilation of the alimentary canal. It has the four typical coats; mucosa,

submucosa, muscular and fibrous. It is the first portion of the canal within the abdominal cavity and is, therefore, the first to have a peritoneal investment. The mucosa is provided with two varieties of glands (peptic and pyloric) which will be described under gastric digestion. This coat lies in prominent folds or *rugæ* upon the subjacent tissues. The muscular coat consists of two principal layers of involuntary muscle, an inner circular and an outer longitudinal layer while an imperfect oblique layer may be found at the cardiac end. The orifice between the œsophagus and the stomach is called the *Cardia* (Fig. 157, *C*). It is guarded by a sphincter. The orifice between the stomach and duodenum is called the *Pylorus* (157, *p*). It is also guarded by a sphincter. At a point about two-thirds of the distance from the cardia to the pylorus is a band of especially strong circular muscles. This has been called by Hofmeister and Schutz the "Sphincter antri pylorici" (Fig. 157, *S. A. P.*). The portion of the stomach between this sphincter and the pylorus is called the *Antrum* (*A*). The middle third of the stomach is called the *preantral* segment (*P. A.*). The antral and preantral segments together make the *Pyloric portion*, while the segment nearest the cardia is called the *Cardiac portion*. The use of these terms will be necessary in the description of the movements of the stomach.

Fig. 158.



Longitudinal section of human small intestine, showing general relation of the folds constituting the valvulæ conniventes to the mucosa and submucous coat; the latter contributes the fibrous core over which the mucosa with its villi and glands extends. (After Piersol.)

5. **The Small Intestine.**—This is a tube of fairly equal caliber lying in coils in the abdominal cavity. It is 16 to 20 feet in length and passes into the cæcum through the ileo-cæcal valve. It is sub-divided into three portions, the duodenum, jejunum and ileum. The four coats of the small intestine differ from those of the stomach principally in the variations of the mucous membrane. The folds of the latter are transverse and are called *valvulæ conniventes*. (See Fig. 158.)

Upon these ridges the mucous membrane presents two important features, (I) the villi which are finger-like projections into the lumen of the intestine, (II) the crypts of Lieberkühn which dip down from the general surface of the mucosa to the muscularis mucosa. The crypts will be described under digestion and the villi under absorption.

Fig. 159.

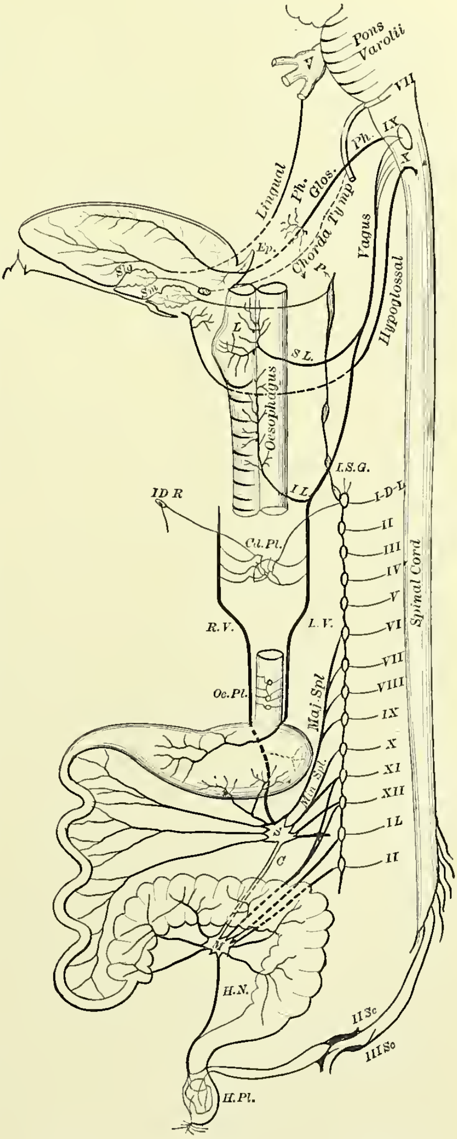


Diagram showing the innervation of the digestive system.

Tributary to the duodenum are two most important glandular bodies, the pancreas and the liver. As the latter has little to do with digestion and much to do with metabolism it will be described in the chapter on metabolism. The pancreas is a tubulo-racemose gland resembling the salivary glands except that the alveoli are tubular. The secreting epithelium of the pancreas is hypoblastic in origin, being derived from the primitive mid-gut by evagination.

6. **The Large Intestine.**—This portion of the intestine consists of the cæcum with its vermiform appendix, the capacious, and transversely constricted colon, and the rectum. The structure of the walls is quite similar to that of the small intestine except that there are *no villi*, and the tubular glands differ from the crypts of Lieberkühn in having a greater proportion of the mucus secreting goblet cells.

2. THE INNERVATION OF THE DIGESTIVE SYSTEM.

Diagram of principal nerves involved in deglutition, secretion and digestion: Showing the lingual branch of the *V* pair, the chorda tympanic branch of the *VII*, the glosso-pharyngeal (*IX*), the vagus (*X*), the hypoglossal (*XII*), the superior cervical ganglion (*S.S.G.*) which sends a branch to the parotid gland (*P*) and one to the base of the tongue which divides and supplies both sublingual (*Slg*) and submaxillary (*Sm*) glands.

The vagus gives off the superior laryngeal (*S.L.*) and the inferior laryngeal branches; gives off branches to the cardiac *plexus*, (*Cd.Pl.*) and, passing down the œsophagus, gives off branches for the œsophageal plexus (*Oe.Pl.*). The left vagus (*L.V.*) supplies the lesser curvature of the stomach while the right (*R.V.*) passes behind the stomach and joins with the large and small splanchnic (*Maj.Spl.* and *Min.Spl.*) to form the solar plexus (*S*). This great plexus supplies the small intestine and sends a large communicating branch (*C*) to the mesenteric ganglion and plexus (*M*). This plexus also receives branches from the *XI* and *XII D*, and the *I* and *II L*. It supplies the large intestine. The hypogastric nerve (*H.N.*), with branches from the *II* and *III* sacral nerves make up the hemorrhoidal plexus about the rectum (*H.Pl.*).

C. SECRETION.

1. GENERAL CONSIDERATIONS.

The tissue-activity of the organism may be conveniently divided into three groups:

(*a*) *Muscular activity*, the general function of muscular tissue, manifesting itself in motion and heat; (*b*) *nervous activity*, the general function of the nervous tissue, including all nervous acts from sensation to reason; (*c*) *glandular activity*, the general function of epithelial and lymphoid tissue including all of those metabolic changes which result in the elaboration of a special mixture either (I) by separating (*selecting*) out of the liquids of the body, compounds which already exist, forming of these a new combination for a special purpose; or, (II) by actually *forming* new substances which may be combined with selected or separated substances to make a special mixture. Of these forms of glandular activity one may cite numerous examples: (I) the elaboration of lymph, urine, perspiration; (II) gastric juice, pancreatic juice, saliva, bile, synovial fluid, lachrymal fluid, sebaceous matter, milk, etc. If one classifies as glandular all those tissues which possess the power of elaboration by *selection* or *formation*, he will find that he has included practically the whole of the derivatives of the hypoblast, special portions of the epiblast, the whole of the derivatives of the splanchnopleure and somatopleure together with the mesoblastic epithelium of the genito-urinary system, and the mesoblastic lymphoid tissue. There seems to be no doubt that all of the tissues enumerated possess this power to a greater or less extent. The glandular activity of the hypoblastic epithelium is specialized in such organs as the pancreas and liver, and such specialized portions of the mucous membrane as the gastric and enteric glands. But the whole epithelium contains a large proportion of the mucus-secreting goblet cells ; some writers stating that any cell of the mucous membrane may become a goblet cell, secrete its mucus and resume its original form as a columnar epithelial cell. Even absorption of the products of digestion from the alimentary canal is not a simple diffusion and filtration but is attended with a marked activity of the epithelium first in certain degree of selection and second in a partial elaboration, changing the peptone to a higher proteid form before it is passed into the capillaries of the portal system, also changing fatty acids and glycerine to fat. That portion of the epiblast which lines the mucous openings of the body, *e. g.*, mouth, nose, anus, and urethra ; and such mucous surfaces as the vulva, prepuce and conjunctiva are richly supplied with mucous glands ; but the goblet cells are absent from all of these locations except the respiratory region of the nasal mucous membrane. In that portion of the epiblast which covers the general surface of the body the glandular activity is subordinated to the function of protection. There are innumerable sebaceous glands and sweat glands but the general surface cannot be called a glandular one.

The endothelial lining of all serous cavities is now conceded to have a general glandular activity. The serous fluid which occupies these cavities is not identical with blood plasma, and though an increased venous pressure leads to an increase of the volume of lymph and serum, these fluids differ quantitatively from plasma. Such a difference cannot be accounted for by purely physical laws of filtration and diffusion, there must be a selective activity on the part of the endothelial tissues. This selective activity manifested by endothelial tissue in general justifies its classification among glandular tissues. In the same category belongs the endothelium of the circulatory system ; though glandular activity has been demonstrated only in the endothelium of capillaries and lymph radicals. The genito-urinary system furnishes numerous examples of glandular activity ; the ovary and testes, and the genital ducts and canals including the oviduct, uterus, vagina, vas deferens, seminal vesicles and prostate ; the kidney and urinary passages. The epithelial tissues of all of the organs enumerated are glandular tissues. It is to be noted here that the secretion of the genital glands is largely composed of cellular elements ; the same may be said of the lymphoid tissues of the circulatory system and of the preliminary secretion (colostrum) of the mammary glands.

2. SECRETION DEFINED.

The term *secretion* may be defined as the special activity of the glandular tissues, or better the elaboration of fluid or semifluid mixtures by selection from the fluids which surround the active cells or by formation from the substance of the active cells. In the secretion of the gastric juice the water and the inorganic salts are selected from the tissue plasma which bathes the glandular epithelium ; the hydrochloric acid is *formed* probably by a reaction between salts of the plasma. It is necessary, however, that these salts be taken into the secreting epithelium and brought under the influence of special forces in order that the reaction may take place. The pepsin of the gastric juice is *formed* from the protoplasm as a product of cell metabolism.

The term secretion in its most general application may be applied to the part which the epithelial cells take in modifying the fluids which filter and diffuse through them. That the absorbing epithelium of the alimentary canal modifies the absorbed liquid is now practically beyond question. In the first place there is a certain selection of the absorbed liquid from the general mixture of digested foodstuffs and in the second place these absorbed substances are modified on their passages through the cells. We have to deal here with a clear case of secretion.

These examples of secretion in its broadest sense fall naturally into two groups : In the case of the gastric juice the elaborated fluid is selected or formed, to be poured out upon the surface of the mucous membrane for a particular use there. In the case of the lymph plasma there is a selection of the substances which are to filter or diffuse through the endothelium from one cavity or vessel into another cavity or vessel, to be retained in the system. In the case of absorption the selected and modified products of digestion are passed into the circulation to be retained and further utilized. We thus have in the gastric juice an example of what has been called an *external secretion,* while in the formation of lymph and the modification of the products of absorption examples of an *internal* secretion.

The hypoblastic epithelium of the liver forms products which not only afford examples of the two kinds of secretion already named, but of a third kind as well. The *bile,* composed of substances which assist in digestion and in absorption, is an *external secretion ;* the *glycogen* formed from the absorbed dextrose and later thrown into the blood as dextrose, is an *internal secretion ;* while the *urea* and related bodies formed in the liver are thrown into the blood, not to be utilized by the system, but to be *secreted* by the kidneys.

In the above presentation of the subject the terms glandular epithelium and secretion have been used in the most general sense. The part which the epithelium plays in the elaboration of the products of digestion are still subjects of controversy. It will be best here to present more in detail the subject of external secretion and the specialized glandular epithelium (*glands*), which elaborate these secretions. Howell defines a gland as "a structure composed of one or more gland-cells epithelial in character, which forms a product—secretion—which is discharged either upon a free epithelial surface (external secretion), such as the skin or mucous membrane, or upon the closed endothelial surface (internal secretion) of the blood and lymph cavities."

The one example of a unicellular gland is the mucus-secreting goblet cell. It is more in harmony with the above presentation of the general physiology of glandular tissues to consider the goblet cells as representing unspecialized glandular tissue cells.

One phase of the process of differentiation which marks the progress of evolution is the development of *glandular organs.* A *glandular organ* or *gland* may be defined as a structure composed of a *specialized* portion of *glandular tissue* which *elaborates* by *selection* or *formation* a *special secretion,* which is discharged either upon an epithelial surface (*external secretion*), or upon an endothelial surface (*internal secretion*).

3. GLANDS.

The following figure illustrates gland types:

Fig. 160.

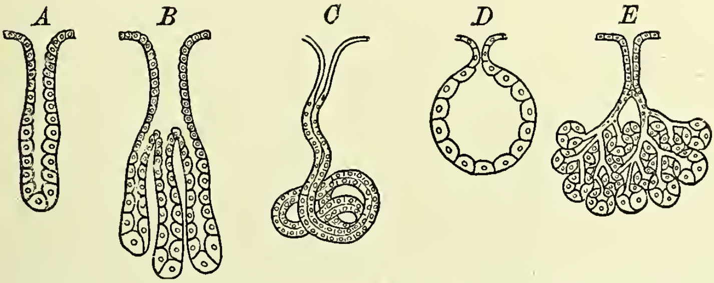
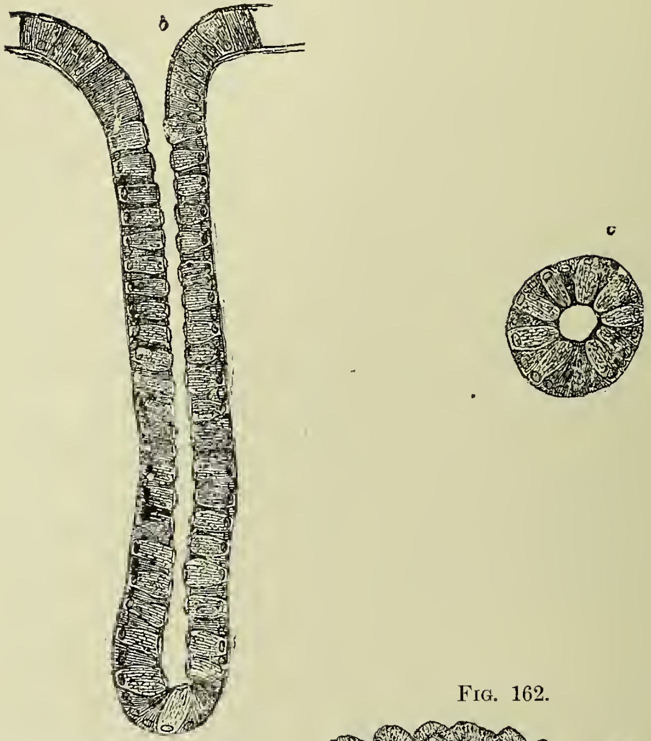


Diagram illustrating the forms of glands: *A*, simple tubular; *B*, compound tubular; *C*, modified (coiled) tubular; *D*, simple saccular; *E*, compound saccular, or racemose. (Piersol.)

As examples of the simple tubular gland one may cite the glands of the large intestine (Fig. 161), the crypts of Lieberkühn, the peptic glands, etc.

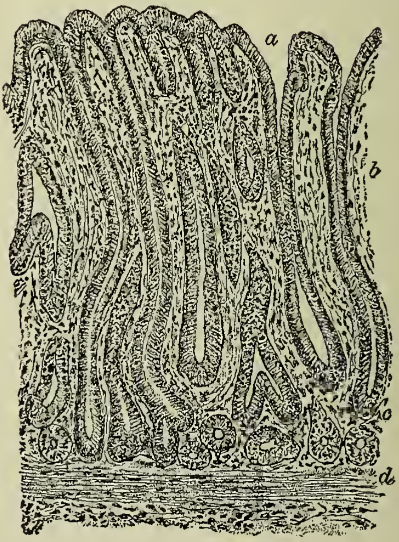
The compound tubular gland is represented in human anatomy by the pyloric glands (Fig. 162) and the glands of Brunner as less complex examples; while the pancreas (Fig. 163), kidney and liver represent compound tubular glands of successively in-

Fig. 161.



Simple tubular gland of large intestine.

Fig. 162.



Pyloric mucous membrane showing compound tubular glands. *a*, mouth; *b*, duct; *c*, compound fundus showing branches cut at various angles; *d*, musc. mucosæ. (After Benda.)

creasing complexity. The sweat glands are coiled tubular glands. The simple saccular glands, though prominent in the amphibia as the mucus-secreting glands of the skin, do not occur in the higher animals. The compound saccular or racemose glands are represented in the human anatomy by the salivary glands (Fig. 164). Some authors classify these as compound tubular glands.

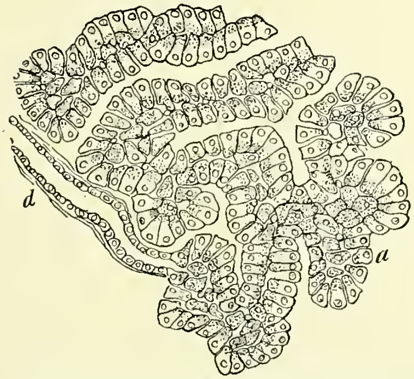
A discussion of the blood and nerve-supply of the various digestive glands, of the histological changes of the glandular epithelium during activity and of the chemical composition of the secretion, will be found in connection with the physiology of the gland.

4. INTERNAL SECRETIONS.

Under this head it is proposed to deal briefly with the *Functions of the Vascular Glands*, also called the ductless glands.[1]

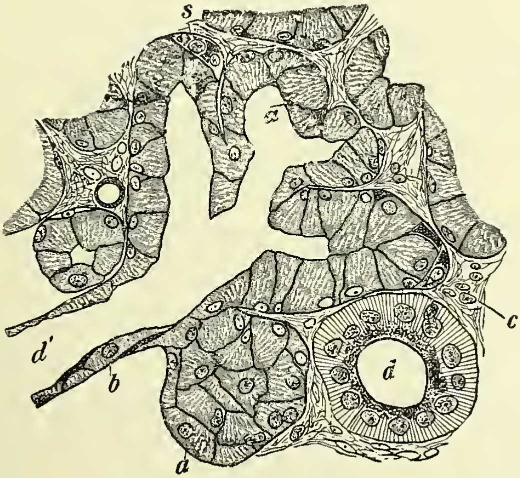
The functions of the vascular glands have been, until quite recently, a matter of somewhat vague speculation. Even now these functions are not by any means clearly established and fully understood; but so much work has been done, experimental and clinical, especially on the thyroid glands, the adrenal capsules and the pituitary body, that the theories advanced as to their functions have the advantage of strong probability.

Fig. 163.



Section of the pancreas of the dog. (Klein.) *d*, termination of a duct in the tubular alveoli, *alv*.

Fig. 164.



Section of human submaxillary gland.

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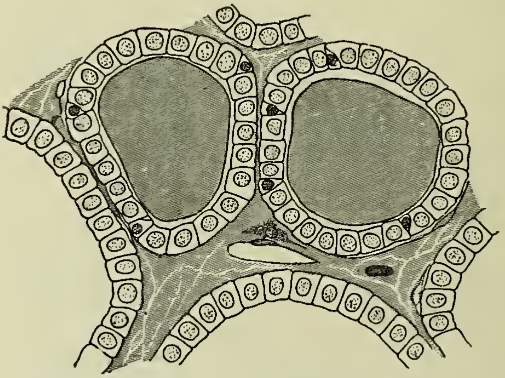
[1] For this section I am indebted to Dr. H. J. Achard, of Roselle, Ill. The limitations of a brief student manual has made it impossible to use more than half of the valuable material received from Dr. Achard.—The Author.

a. The Thyroid Gland.

The thyroid gland is situated at the upper part of the trachea and consists of two lateral lobes, placed one on each side of that tube, and connected by a narrow transverse portion, the isthmus. The thyroid is of a brownish-red color. Its weight varies from one to two ounces. It is larger in females than in males, and becomes slightly increased in size during menstruation and after maternity. It occasionally becomes enormously hypertrophied, constituting the disease called bronchocele or *goitre*.

The accessory thyroids, or *parathyroids*, seem to occur in all mammals. One of these bodies is attached to the external or posterior surface of the lateral lobes of the thyroid; in some animals (dog, cat, rabbit, etc.), there is an additional lobe on each side, imbedded in the substance of the thyroid proper. Histologically the parathyroids do not resemble the thyroid gland (vide infra). They present a general appearance of embryological tissue, and, for this reason, have been regarded as an immature form of thyroid tissue, which, under the stimulus of increased functional activity, is capable of developing into normal thyroid tissue.

Fig. 165.



Section of the thyroid gland of a child. Two complete vesicles and portions of others are represented. The vesicles are filled with colloid, which also occupies the interstitial spaces. In the middle of one of the spaces a blood vessel is seen cut obliquely, and close to it is a plasma-cell. Between the cubical epithelium-cells smaller cells like lymph-corpuscles are here and there seen. (Schaefer.)

There is, however, no satisfactory evidence that such a transformation may take place. The histological and embryological evidence seems to indicate that the two tissues are not only fundamentally different in structure, but probably also different in origin.

The thyroid body is invested by a thin capsule of connective tissue, which projects into its substance and imperfectly divides it into masses of irregular form and size. When the organ is cut into it is seen to be made up of a number of closed vesicles containing a yellow glairy fluid and separated from each other by intermediate connective tissue. Each vesicle is lined by a single layer of epithelium, the cells of which, though differing somewhat in shape in different animals, have always a tendency to assume the columnar form. Between the epithelial cells exists a delicate reticulum. The vesicles are of various sizes and shapes, and contain as a normal product a viscid, homogeneous, semi-fluid, slightly yellowish material, which frequently contains blood, the red blood corpuscles of which are found in it in various stages of disintegration and decolorization, the yellow tinge being probably due to the hæmoglobin, which is thus set free from the colored corpuscles.

The thyroid gland is for the animal economy a most important, indeed, necessary, organ. Its removal or destruction is followed by serious disturbances of nutrition, and is immediately or ultimately fatal, because products of the normal metabolism attack and harm the central nervous system, so that nervous disturbances and depression occur as well as disturbances of nutrition (tetanus and cachexia). The reintroduction of thyroid material (by grafting, subcutaneous or intervascular injection, or absorption from the alimentary canal), causes an amelioration, or even an entire removal of all toxic symptoms.

It follows from the foregoing that the thyroid tissue produces normally some material which is in some way essential to the nutrition of the body, and which acts as an antitoxic to those products of normal metabolism which produce tetanus and cachexia in thyroidectomized animals. Such a material has been isolated by Baumann, and is called thyroiodin, or iodothyrin. It is an organic compound of iodin, is produced by the thyroid gland from traces of iodin contained in the food and carried into the blood. According to the experiments of Roos, it preserves the beneficial effects of thyroid tissue, and acts like the latter in thyroidectomized animals.

The fact that extracts of thyroid tissue, or iodothyrin, when absorbed into the blood, ameliorate or remove the evil effects resulting from a loss of function of the thyroid gland seems to prove that the normal function of the thyroid is not merely to excrete poisonous material after the manner of the kidneys. It indicates on the contrary that these tissues act normally by giving off a material to the blood which in some way affects favorably the nutrition of all or a part of the tissues of the body. Histological research shows that, as far as the thyroid bodies proper are concerned, this secretion is contained in the so-called colloidal material which accumulates in the interior of the vesicles, and that the mechanism of secretion consists in a rupture of the walls of the vesicles at some point, whereby the contents are discharged into the surrounding lymph spaces.

The most important fact to be discovered is the manner of action of this secretion upon the tissues of the body. There are two hypotheses proposed:

(I) The function of the thyroid secretion is antitoxic, *i. e.*, it antagonizes an unknown toxic substance supposed to be formed in the body in the course of normal metabolism. When the thyroid tissues are removed, this poisonous material, imperfectly excreted, accumulates in the blood and produces the fatal symptoms of thyroidectomy by auto-intoxication.

(II) The secretion of the thyroid acts normally by promoting or regulating the metabolism of other parts of the body, particularly perhaps the nervous tissues.

As yet no decisive or even probable proof for either view has been given, and in working out the problem there are two great facts to be explained: (I) that complete removal of the thyroid tissue causes malnutrition, affecting, it seems, especially the central nervous system; and (II) that the injection or ingestion of thyroid extracts in this condition restores metabolism more or less completely to a normal state.

An interesting phase in the physiology of the thyroid is the functional relation between the thyroid and the parathyroid bodies.

Gley was the first to prove the physiological importance of the parathyroids. He showed that in rabbits complete extirpation of the thyroid lobes alone is not followed by fatal results, as long as the parathyroids remain. Removal of both thyroid and parathyroid tissue is in most cases followed by typical symptoms of complete thyroidectomy, resulting in the death of the animal. The latter result has been contested by some observers, but renewed investigations have demonstrated its accuracy. Gley's explanation is that after removal of the thyroid its function is vicariously assumed by the parathyroids, and his conclusion: that the functional value of the two tissues is identical. But recent work tends to throw doubt on this conclusion. Vassale and Generali state that in dogs and cats the removal of all four parathyroids causes acute symptoms of complete thyroidectomy and finally death, although the thyroid proper be practically uninjured; but the complete removal of the thyroid lobes is not immediately injurious, if the parathyroids (even only one) are left. They contend that the result usually attributed to the extirpation of the thyroid is really due to the simultaneous removal of the parathyroids.

This result has been partly confirmed by Rouxeau and Gley. Moussu, from a study of over 150 thyroidectomies and parathyroidectomies, arrives at these conclusions:

(I) "The organs of the thyroid system have two distinct functions, one thyroidal and one parathyroidal. The thyroids do not act vicariously for the parathyroids, and *vice versa.*

(II) "The thyroid function is the same for all domestic animals and for birds. Its suppression has always the same result, viz.: development of *cretinism,* if it is caused under identical conditions.

(III) "Cretinism occurs only in the young. It is the more acute the earlier the subjects are operated on.

(IV) "In adults thyroidectomy does not cause acute symptoms, not even in carnivora. The operation is generally survived for a long period, but may be followed by progressive cachexia or by myxœdema.

(V) "The *parathyroid function is for the most vital conditions of life indispensable.* It seems to influence immediately the nutrition of tissues.

(VI) "Its suppression causes rapid death if total, alarming disturbances if partial.

(VII) "The symptoms of parathyroid insufficiency seem to show certain analogies with those of the Basedow's disease.

(VIII) "The acute symptoms, such as tetanus, tachycardia, dyspnœa or polypnœa, etc., following operations on the goitre in man are parathyroid symptoms.

(IX) "The chronic symptoms, such as lowering of temperature, weakening of the intellectual faculties, myxœdema, etc., are exclusively thyroid symptoms.

(X) "Strumiprive cachexia must develop fatally if thyroidectomy is performed during infancy and adolescence.

"In all operations on the thyroid organs the first duty of the surgeon is to look for and *to respect the parathyroids in all cases.*"

Von Cyon has made a full and exhaustive study of the relation of the thyroid gland and the heart. He states that a suppression of the thyroid function (through illness or extirpation) and likewise an increase of the functional activity (injection of iodothyrin) have an "immense" influence on the entire nervous system of heart and blood vessels. He proves that the vagus participates in the innervation of the thyroid gland, or is, at least, closely connected with it, and offers, in his discussion of the hypotheses on the functions of the thyroid (vide supra) the following conclusions:

(XI) "The function of the thyroid gland is to make harmless the salts of iodin, which have a toxic effect on the vagi and sympathetic nerves, by converting them into an organic compound: the *iodothyrin,* which has a stimulating effect on the same nerves, and increases their power.

(XII) "The thyroid gland functions mechanically as a *safeguard for the brain against engorgement.* In a sudden increase of blood-pressure, whether from increased activity of the heart or from increased resistance of the peripheral blood-currents, the thyroid gland is capable of passing a large amount of blood in a short time through its vessels, taking it thus directly from the arterial back into the venous circulation and preventing its entrance into the cerebral circulation."

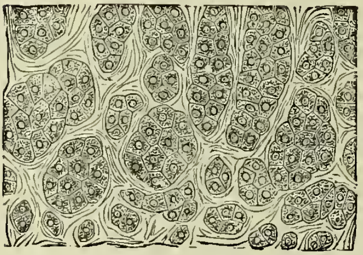
Other investigators confirm these theories of Gley and von Cyon.

b. The Suprarenal Capsules.

The suprarenal capsules, or bodies, are found constantly in all classes of vertebrates, and seem, therefore, to be organs of fundamental importance. They are two small flattened glandular bodies, of a yellowish color, situated at the back part of the abdomen, behind the peritoneum, and immediately in front of the upper part of either kidney.

On making a perpendicular section the glands are seen to consist of two substances—external or cortical, and internal or medullary. The former, which constitutes the chief part of the organ, is of a deep-yellow color and consists chiefly of narrow columnar masses placed perpendicularly to the surface. The medullary substance is soft, pulpy, and of a dark-brown or black color.

FIG. 166.



Field from the outermost layer of the cortical substance of a suprarenal body. (SCHAEFER after EBERTH.)

Brown-Séquard stated in 1856 that extirpation of both suprarenals is usually fatal to the animal, and more rapidly fatal than the removal of both kidneys. Recent experiments seem to corroborate this statement. The fact that in some species of animals accessory suprarenals occur may explain why extirpation is not always fatal.

On removal of only one of the bodies no noticeable disturbances have been observed. After complete removal, with ultimately fatal results, the prominent symptoms were: Extreme muscular weakness, asthenia, and, in the case of dogs examined during this period, a great fall in the blood-pressure, together with a feeble heart-beat, have been ascertained. It is worthy of notice that in Addison's disease these symptoms occur, together with the familiar pigmentation; the explanation of these symptoms is, however, still *sub judice.*

The effects of injections of suprarenal extracts in living animals, on the vascular and respiratory organs, have recently been studied by Oliver and Schaefer, and by Cybulski and Szymonowicz.

Extracts of the medullary portion of the suprarenals, injected into the veins of an animal, caused pronounced slowing of the heart beat and a large rise of blood-pressure. If the animal was first given atropin to paralyze the inhibitory nerves to the heart, or, if the vagi were previously cut, the injection was followed usually by a marked quickening instead of slowing of the heart beat, and by a greater rise of blood-pressure. The organs of respiration were not affected so seriously. A temporary slowing and shallowing of the respirations could usually be noticed. According to Oliver and Schaefer the heart is influenced by the direct action of the extract upon the cardio-inhibitory center. The enormous rise of blood-pressure is due to constriction of the arterioles.

Blood drawn from the suprarenal vein and injected into the circulation of normal animals causes the same symptoms, though less intense, as injection of extract, while blood drawn from other veins has no effect.

From the above it seems certain that a material formed by the secretory activity of the gland cells occurs normally in the venous blood flowing from the gland. Probably it is a normal product of metabolism of the medullary cells of the gland, and is secreted and discharged directly into the blood. It must, therefore, exert continually *a stimulating effect upon the heart and blood vessels. This assumption is confirmed by the fact that after complete extirpation of both glands the blood-pressure is greatly depressed.*

The normal function of the suprarenal bodies consists in furnishing this stimulating substance to the blood. It is believed that its effects are exerted mainly on the muscular tissue, at any rate it has a general tonic or augmenting action on all varieties of muscles found in the body, or perhaps the effect may be on the nerve centers controlling the muscular action rather than on the tissues directly. It is impossible at present to decide the exact mode of action.

c. Hypophysis Cerebri.

The hypophysis cerebri (or pituitary body) is a small reddish-gray mass, weighing from five to ten grains. It is very vascular and consists of two lobes, separated from one another by a fibrous lamina. Of these, the anterior is the larger, of an oblong form and somewhat concave behind, where it receives the posterior lobe, which is round. The two lobes differ both in origin and structure. The anterior lobe, of a dark, yellowish-gray color, is developed from the ectoderm of the buccal cavity, and resembles to a considerable extent, in microscopic structure, the thyroid body. It is thus a glandular structure. According to Haller it cannot be called strictly a ductless gland, since it possesses an imperfectly developed system of ducts opening between the dura and pia mater. It is evidently a secretory structure, and the fact that the secretion is discharged between the meningeal membranes suggests some special connection with the physiology of the brain. The posterior lobe is developed by an outgrowth from the embryonic brain, and during fetal life contains a cavity which communicates through the infundibulum with the cavity of the third ventricle. It is always small and has the appearance of a rudimentary organ.

The clinical observations as to the function of the pituitary body have been limited to the glandular lobe. In many cases of acromegalia this presents pathological changes. Extracts of the gland have been used in some cases and some of the disagreeable features have shown amelioration. But the evidence at hand is not satisfactory and the nature of the connection between acromegalia and the functional disturbance of the hypophysis, if any exists, needs more complete investigation.

Howell has made experiments with extracts of both lobes of the hypophyses (of sheep) separately. Injections of extracts of the glandular lobe gave little or no effect, while *injections of extracts of the infundibular lobe had a distinct and remarkable effect on the heart rate and blood-pressure, which resembles in some respects, and differs in others from that of suprarenal extracts.*

Extracts injected in normal animals with vagi intact caused a pronounced slowing of the heart beat, similar to that from suprarenal extracts, but lasting a much longer time. The heart beats were not only slowed, but considerably augmented in force. The blood-pressure rises to a considerable extent, owing apparently to the peripheral constriction of blood vessels. If the dose was a maximal one, and followed too quickly by a second injection, there was little or no effect, but if the dose was not too strong, and sufficient time was allowed for the effects to wear off, they could be repeated. With each repetition the effects decrease progressively in intensity.

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W. H. HOWELL. *Internal secretions, considered in their physiological, pathological and clinical aspects ; physiology of internal secretions.* Tr. Cong. Am. Phys. and Surg., N. Haven, 1897, iv.
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MOUSSU. *Recherches sur les funetions thyroidienne et parathyroidienne.* Rec. de Méd. Vét. Paris, 1897 ; 8-s.; iv.
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D. CHEMICAL INTRODUCTION.

1. FUNDAMENTAL CARBON COMPOUNDS.

One cannot gain a definite idea of the metabolic processes of nutrition without knowing the chemical composition of the body and of foodstuffs, and following, as closely as may be, the chemical reactions which take place during the processes of digestion, and the processes of constructive and of destructive metabolism.

The author proposes to summarize here a few of the facts of chemistry that may be convenient for reference during the study of the succeeding chapters on nutrition.

The chemistry of the carbon compounds is the basis for physiological chemistry.

The compounds of carbon with hydrogen form the basis for the consideration of all of the higher carbon compounds.

The simplest compound of carbon and hydrogen is marsh gas or *methane*, CH_4.

A clear notion of the relations of various compounds involved in nutrition can only be gained through a study of the structural formulæ of those compounds. Let us, therefore, use the structural formulæ as far as possible.

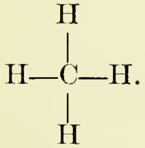
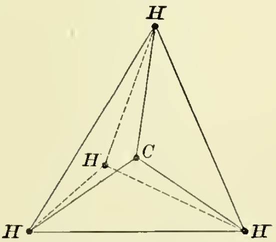
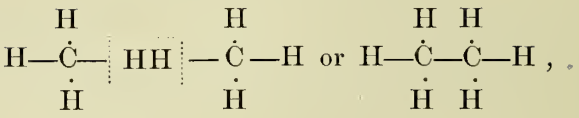
The structural formula of methane is :  $\begin{array}{ccc} & H & \\ & | & \\ H— & C & —H. \\ & | & \\ & H & \end{array}$ As these five atoms must be conceived as occupying positions in tri-dimensional space, we may assume that they are symmetrically arranged with the carbon atom in the center. That gives us a tetrahedron with each hydrogen atom equidistant from each other hydrogen atom. The space relations of the atoms being as yet largely conjectural we will be content with representing the molecule on a plane surface. All of the hydrogen atoms are displacable. They may be displaced singly by monads or monivalent radicles, or by two diads, etc., etc.

FIG. 167.



Space relations of the atoms in methane.

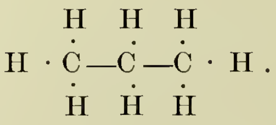
One fundamental method of combination of carbon atoms is through dropping two hydrogen atoms :



$$\mathrm{H{-}\underset{H}{\overset{H}{C}}{-}\ HH\ {-}\underset{H}{\overset{H}{C}}{-}H}\ \text{or}\ \mathrm{H{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}H},$$

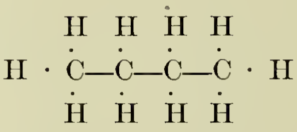
This compound is called *Ethane*, and may be written C_2H_6 or $CH_3—CH_3$.

The third carbon compound in the series is *Propane*, written C_3H_8; $CH_3—CH_2—CH_3$ or:



$$\mathrm{H\cdot\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}\cdot H}.$$

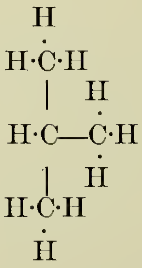
The fourth member of the series is *Butane*: C_4H_{10}; $CH_3—CH_2—CH_2—CH_3$ or:



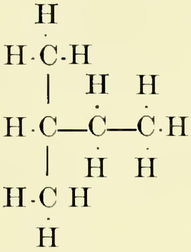
$$\mathrm{H\cdot\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}\cdot H}$$

The series may be continued through *Pentane, Hexane, Heptane, Octane, Dodecane* and *Hecdecane*, which are called the normal paraffins.

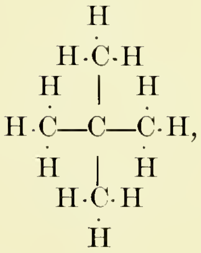
If one study the structural formula of butane, he finds that the same number of atoms may be differently arranged and still satisfy all of the bonds:



The two forms of butane which exist can only be accounted for in this way. This property of the molecule is called *Isomerism*. The first butane is *normal butane*, the second *isobutane*. As the series advances the possibility of isomerism rapidly increases. Besides the normal pentane above given there are: *Isopentane*,—

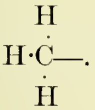


and *Mesopentane*

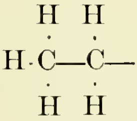


note that all of these forms of pentane have the formula C_5H_{12}. It is hardly necessary to say that this property gives rise in the higher carbon compounds to an almost interminable series of combinations.

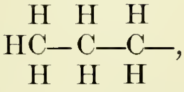
Let us now turn our attention to some of the derivatives of the series of hydrocarbons. If one of the atoms of hydrogen be removed from CH_4 a monad radicle methyl will result: *Methyl* =



CH_3—; $\overset{H}{\underset{H}{H\cdot C}}$—. In a similar way arise the *monad radicles:*



Ethyl = C_2H_5— ; CH_3—CH_2— ; $H\cdot\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-$



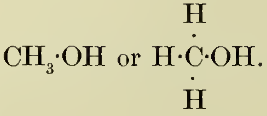
Propyl = C_3H_7—; CH_3—CH_2—CH_2— ; $H\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-$,

Butyl = C_4H_9— ; *Pentyl* = C_5H_{11}— ; *Hexyl* = C_6H_{13}— ; etc.

When one of the monad radicles takes the place of one of the hydrogen atoms of a molecule of water an alcohol results:

$$\left.\begin{matrix}CH_3\\H\end{matrix}\right>O \text{ methyl alcohol.}$$

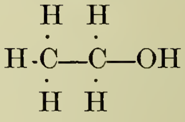
Another way of representing the matter is to conceive one of the atoms of hydrogen of the hydrocarbon (methane, ethane, etc.) to be exchanged for OH or *hydroxyl* which may be written :



$$CH_3\cdot OH \text{ or } \begin{array}{c}H\\ \cdot\\ H\cdot C\cdot OH.\\ \cdot\\ H\end{array}$$

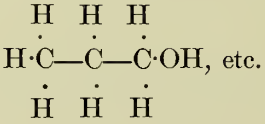
In the same way arises the series of *primary monatomic alcohol* :

Ethyl alcohol,—$C_2H_3 \cdot OH$; CH_3—CH_2OH ;



$$\begin{array}{cccc} & H & & H\\ & \cdot & & \cdot\\ H\cdot & C & — & C—OH\\ & \cdot & & \cdot\\ & H & & H\end{array}$$

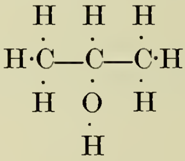
Propyl alcohol—$C_3H_7 \cdot OH$; CH_3—CH_2—CH_2OH ; or :



$$\begin{array}{cccccc} & H & & H & & H\\ & \cdot & & \cdot & & \cdot\\ H\cdot & C & — & C & — & C\cdot OH, \text{ etc.}\\ & \cdot & & \cdot & & \cdot\\ & H & & H & & H\end{array}$$

In the propyl alcohol it is evident that the hydroxyl may displace a hydrogen from the central carbon atom instead of one of the end atoms giving the

formula



$$\begin{array}{cccccc} & H & & H & & H\\ & \cdot & & \cdot & & \cdot\\ H\cdot & C & — & C & — & C\cdot H\\ & \cdot & & \cdot & & \cdot\\ & H & & O & & H\\ & & & \cdot & & \\ & & & H & & \end{array}$$

or secondary propyl alcohol.

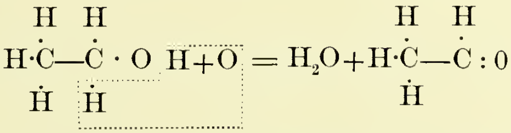
This is the first one of a series of *secondary monatomic alcohols.*

Table showing the normal paraffin series with the corresponding radicles and primary monatomic alcohols :

THE PARAFFINS.	RADICLES.	ALCOHOL.
General Formulæ : C_nH_{2n+2} *or* $(CH_3)_2(—CH_2)_{n-2}$	C_nH_{2n-1} *or* $CH_3—(CH_2)_{\overline{n-2}}CH_2—$	$C_nH^{2n-1} \cdot OH$ *or* $CH_3\,(CH_2)_{\overline{n-2}}CH_2OH$
Methane, $CH_3—H$	Methyl, $CH_3—$	Methyl alcohol : $H\cdot CH_2\cdot OH$
Ethane, $CH_3—CH_3$	Ethyl, $CH_3—CH_2—$	Ethyl alcohol : $CH_3—CH_2—OH$
Propane, $CH_3—CH_2—CH_3$	Propyl, $CH_3—CH_2—CH_2—$	Propyl alcohol : $CH_3—CH_2—CH_2OH$
Butane, $CH_3(CH_2)_2CH_3$	Butyl,$CH_3—(CH_2)_2—CH_2—$	Butyl alcohol : $CH^3—(CH_2)_2—CH_2OH$
Pentane, $CH_3—(CH_2)_3—CH_3$	Pentyl, $CH_3—(CH_2)_3—CH_2—$	Pentyl alcohol : $CH_3—(CH_2)_3—CH_2OH$
Hexane, $CH_3—(CH_2)_4—CH_3$	Hexyl, $CH_3—(CH_2)_4—CH_2—$	Hexyl alcohol : $CH^3—(CH_2)_3—CH_2OH$
Heptane, $CH_3—(CH_2)_5—CH_3$	Heptyl, $CH_3—(CH_2)_5—CH_2—$	Heptyl alcohol: $CH_3—(CH_2)_5—CH_2OH$
Octane, $CH_3—(CH_2)_6—CH_3$	Octyl, $CH_3—(CH_2)_6—CH_2—$	Octyl alcohol : $CH_3—(CH_2)_6—CH_2OH$

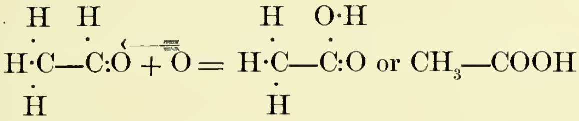
Any primary alcohol when oxidized step by step undergoes the following change as the first step :

Ethyl alcohol + oxygen = water + ethyl aldehyde :



$$H\cdot\overset{H}{\underset{H}{C}}—\overset{H}{\underset{H}{C}}\cdot O\ H+O = H_2O+H\cdot\overset{H}{\underset{H}{C}}—\overset{H}{C}:O$$

The second step consists in the addition of an oxygen atom to the molecule thus: ethyl aldehyde + oxygen = acetic acid (number 2 in the fatty acid series).



$$H\cdot\overset{H}{\underset{H}{C}}—\overset{H}{C}:O + O = H\cdot\overset{H}{\underset{H}{C}}—\overset{O\cdot H}{C}:O \text{ or } CH_3—COOH$$

The group COOH is called the *carboxyl* group.

Table showing the *primary monatomic alcohols* and the corresponding oxidation products—aldehydes and fatty acids.

ALCOHOLS.	ALDEHYDES.	FATTY ACIDS.
$CH_3—(CH_2)_{\overline{n-2}}CH_2\cdot OH$	$CH_3—(CH_2)_{\overline{n-2}}CHO$	$CH_3\cdot(CH_2)_{\overline{n-2}}COOH$
Methyl alcohol : $H\cdot CH_2\cdot OH$	Methyl aldehyde : $H\cdot CHO$	Formic acid : $H\cdot COOH$
Ethyl alcohol : $CH_3—CH_2\cdot OH$	Ethyl aldehyde : $CH_3—CHO$	Acetic acid : $CH_3—COOH$
Propyl alcohol : $CH_3—(CH_2)_1—CH_2\cdot OH$	Propyl aldehyde : $CH_3—(CH_2)_1—CHO$	Propionic acid : $CH_3—(CH_2)_1—COOH$
Butyl alcohol : $CH_3—(CH_2)_2—CH_2\cdot OH$	Butyl aldehyde : $CH_3—(CH_2)_2—CHO$	Butyric acid :[1] $CH_3—(CH_2)_2—COOH$
Pentyl alcohol : $CH_3—(CH_2)_3—CH_2\cdot OH$	Pentyl aldehyde : $CH_3—(CH_2)_3—CHO$	Pentylic acid :[1] $CH_3—(CH_2)_3—COOH$
—	—	Hexylic acid : $CH_3—(CH_2)_4—COOH$
		Heptylic acid : $CH_3—(CH_2)_5—COOH$
		Octylic acid : $CH_3—(CH_2)_6—COOH$
		Nonylic acid : $CH_3—(CH_2)_7—COOH$

Higher normal fatty acids whose formulæ may be written from the above generalized formula are: 10th Capric acid, 12th Lauric acid, 14th Myristic acid, 16th Palmitic, 17th Margaric, 18th Stearic, 20th Arachnic, 30th Melissic acid.

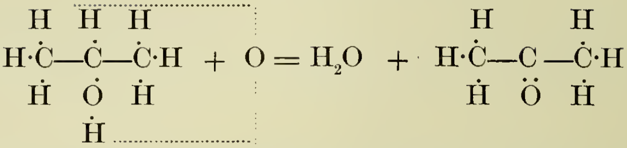
The oxidation of the primary monatomic alcohols gives rise to a series of *aldehydes* of the *monatomic alcohols.*

The oxidation of the secondary monatomic alcohols gives rise to a series of *ketones.* The first step in the oxidation may be represented thus :

Secondary propyl alcohol + O = H_2O + ketone of secondary propyl alcohol.

---

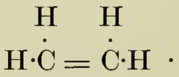
[1] Corresponding to butyric acid is isobutyric acid, written : $(CH_3)_2—CH—COOH$; and corresponding to pentylic acid is its isomere valerianic acid $(CH_3)_2—CH—CH_2—COOH$.



$$\begin{array}{cccc} & H & H & H \\ H\cdot & C & —C & —C\cdot H \\ & H & O & H \\ & & H & \end{array} + O = H_2O + \begin{array}{ccc} H & & H \\ H\cdot C & —C & —C\cdot H \\ H & O & H \end{array}$$

Note that the ketone contains two methyl radicals joined by CO. Its chemical name is *Dimethyl ketone.* The ketone derived from secondary butyl alcohol has the formula : $CH_3—CH_2—CO—CH_3$, and may be called *Methylethyl ketone.* A further oxidation breaks up the ketone into its elements yielding acids which contain fewer atoms of carbon than the secondary alcohol from which they were derived.

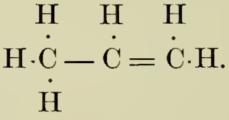
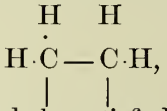
The Diatomic Alcohols or Glycols.—The combination of two carbon atoms in the paraffin-ethane ($CH_3—CH_3$) may, under certain conditions, be brought about with fewer than six hydrogens, yet all of the bonds of carbon will be satisfied. The following formula shows the structure of this molecule :

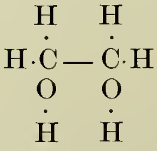


$$\mathrm{H\cdot\overset{H}{C}=\overset{H}{C}\cdot H}\ \cdot$$

It is called *Ethylene,* has the general formula C_nH_{2n}. It is also called *olefiant gas,* and is the first of a series of *Olefines.*

The second member of the series is *Prophylene* with the formula

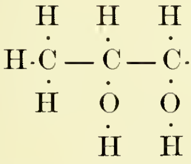
$CH_3 — CH = CH_2$;  $\mathrm{H\cdot\underset{H}{\overset{H}{C}}-\overset{H}{C}=\overset{H}{C}\cdot H}$. The third member of the series is Butylene : $CH_3 — CH_2 — CH = CH_2$. The olefines have two bonds satisfied in such a way that they may readily be loosed from their connection in the olefine and take up other monad atoms or radicals. For example in ethylene ($CH_2 = CH_2$) the double bond which joins the carbons may be conceived to stand thus :  $\mathrm{H\cdot\underset{|}{\overset{H}{C}}-\underset{|}{\overset{H}{C}}\cdot H}$, and require union with monads. If these two bonds be satisfied with hydroxyl we have :



$$\mathrm{H\cdot\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{\underset{H}{O}}{\overset{H}{C}}\cdot H}$$

ethylene alcohol or glycol.

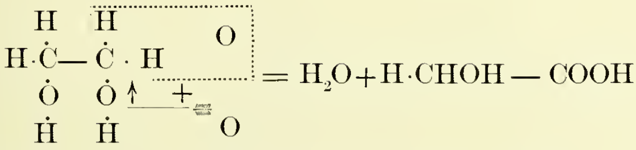
In the same way we may derive propylene alcohol or propylene glycol:



$$\begin{array}{ccccccc} & H & & H & & H & \\ H\cdot & C & - & C & - & C & \cdot H \\ & H & & O & & O & \\ & & & H & & H & \end{array}\text{, or } CH_3 - CHOH - CH_2OH.$$

Remember that the oxidation of the primary monatomic alcohols leads to the formation of a series of normal fatty acids. The oxidation of the primary diatomic alcohols or primary glycols leads to the formation of two series of acids:

1. **The Lactic Acid Series.**—Ethylene glycol $+ O_2 = H_2O +$ glycollic acid.



$$\begin{array}{ccccccc} & H & & H & & & \\ & & & & & & O \\ H\cdot & C & - & C & \cdot H & & \\ & O & & O & \uparrow & + & \\ & H & & H & & & O \end{array} = H_2O + H\cdot CHOH - COOH$$

In a similar way lactic acid is derived from propylene.

2. **The Oxalic Acid Series:**

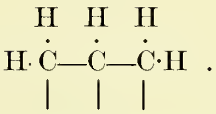
$$\text{Ethylene glycol} + 2O_2 = 2H_2O + \text{oxalic acid.}$$
$$CH_2OH—CH_2OH + 2O_2 = 2H_2O + COOH—COOH.$$

On the next page is a table showing the Olefines, the Primary Diatomic Alcohols, the Lactic Acid Series and Oxalic Acid Series with the general (*a*) quantitative and (*b*) structural formulæ:

	Olefines.	Alcohols : Glycols.	Acids (Monobasic).	Acids (Diabasic).
(a)	C_nH_{2n}	$C_nH_{2n}(OH)_2$	$C_nH_{2n}O_3$	$C_nH_{2n-2}O_4$
(b)	$CH_3-(CH_2)_{\overline{n-3}}CH=CH_2$	$CH_3-(CH_2)_{\overline{n-3}}CHOH=CH_2OH$	$CH_3-(CH_2)_{\overline{n-3}}CHOH-COOH$	$COOH-(CH_2)_{\overline{n-3}}COOH$
I.	——	——	[Carbonic Acid : $OH \cdot COOH$]	——
II.	Ethylene. $H \cdot CH=CH_2$	Ethylene glycol : Glycol. $H \cdot CHOH-CH_2OH$	Glycollic acid : $H \cdot CHOH \cdot COOH$	*Oxalic Acid*: $COOH-COOH$
III.	Propylene. $CH_3-CH=CH_2$	Propylene glycol: $CH_3-CHOH-CH_2OH$	*Lactic Acid* : $CH_3 \cdot CHOH \cdot COOH$	Malonic acid: $COOH-CH_2-COOH$
IV.	Butylene. $CH_3-CH_2-CH=CH_2$	Butylene glycol: $CH_3-CH_2-CHOH-CH_2OH$	Hydroxy-butyric acid : $CH_3 \cdot CH_2 \cdot CHOH \cdot COOH$	Succinic acid: $COOH-(CH_2)_2-COOH$
V.	Pentylene or Amylene. $CH_3-(CH_2)_2-CH=CH_2$	Amylene glycol: $CH_3-(CH_2)_2-CHOH-CH_2OH$	Hydroxy valeric acid : $CH_3-(CH_2)_2-CHOH-COOH$	Pyrotartic acid: $COOH-(CH_2)_3-COOH$
VI.	Hexylene. $CH_3-(CH_2)_3-CH=CH_2$	Hexylene glycol: $CH_3-(CH_2)_3-CHOH-CH_2OH$	Leucic acid : $CH_3- CH_2)_3-CHOH-COOH$	Adypsic acid: $COOH-(CH_2)_4-COOH$
VII.	Heptylene. $CH_3-(CH_2)_4-CH=CH_2$	——	——	Pimelic acid: $COOH-(CH_2)_5-COOH$
VIII.	Octylene. $CH_3-(CH_2)_5-CH=CH_2$	Octylene glycol: $CH_3-(CH_2)_3-CHOH-CH_2OH$	——	Suberic acid.
IX.				Azelaic acid.
X.				Sebacic acid.

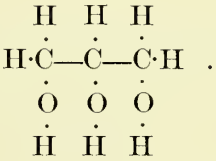
The Triatomic Alcohols and Derivatives.

The series of triatomic alcohols begins with the tri-carbon radicle *propenyl* which is derived from propane:



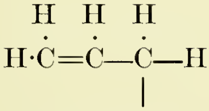
$$H\cdot\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}\cdot H\ .$$

When the three open bonds are satisfied with hydroxyl we have propenyl alcohol, glycerol or glycerine:



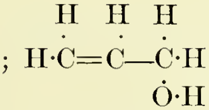
$$H\cdot\overset{H}{\underset{\underset{H}{O}}{C}}-\overset{H}{\underset{\underset{H}{O}}{C}}-\overset{H}{\underset{\underset{H}{O}}{C}}\cdot H\ .$$

It is evident that in the propenyl radical two of the open bonds may be reciprocally satisfied giving rise to a monad radical *allyl* and its corresponding alcohol:



$$H\cdot\overset{H}{C}=\overset{H}{C}-\overset{H}{\underset{|}{C}}-H$$

Allyl radical.



$$;\ H\cdot\overset{H}{C}=\overset{H}{C}-\overset{H}{\underset{O\cdot H}{C}}\cdot H$$

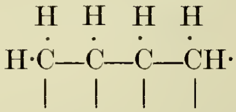
Allyl alcohol.

The acid series corresponding to this alcohol is called *Oleic Acid Series,* oleic acid being the XVIII member of the series which begins with III, acrylic acid.

Table showing the Triatomic Alcohol series and some of the monad derivatives of the series, with the generalized quantitative and (structural) formulæ.

No.	TRIAD HYDROCARBON.	ALCOHOL.	MONAD HYDROCARBON.	OLEIC ACID SERIES.
	C_nH_{2n-1}	$C_nH_{2n-1}(OH)_3$	C_nH_{2n-1}	$C_nH_{2n-2}O_2$
	$CH_3(CH_2)n-4$ $(CH_2)CH_2$	$CH_3-(CH_2)n-4$ $(CHOH)_2CH_2OH$	$CH_3-(CH)_{2n-4}$ $-(CH)_2-CH_2$	$CH_3-(CH_2)n-4$ $-(CH)_2-COOH$
III.	Propenyl. $H\cdot\underset{|}{CH}-\underset{|}{CH}-\underset{|}{CH_2}$	Glycerol. $H\cdot CHOH-CHOH-$ CH_2OH	Allyl. $H\cdot CH=CH-\underset{|}{CH_2}$	Aceylic acid. $H\cdot CH=CH-COOH$
IV.	——	——	——	Crotonic acid. $CH_3-(CH)_2COOH$
XVIII.	——	——	——	*Oleic Acid.* $CH_3-(CH_2)_{14}-(CH)_2$ $COOH$ or $C_{18}H_{34}O_2$

The tetratomic alcohols begin with the derivative of butane having the formula:



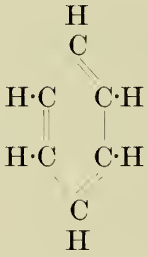
$$\mathrm{H{\cdot}\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}H{\cdot}}$$

When each of these open bonds is satisfied we have the tetrad alcohol *Erythrol* $CH_2OH—(CHOH)_2—CH_2OH$. *The hexatomic alcohols* begin with mannitol or mannite whose formula is $CH_2OH—(CHOH)_4—CH_2OH$.

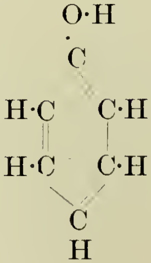
Benzole and its Derivatives.

The carbon compounds thus far considered are arranged with the carbon atoms forming a chain. There is some departure from this rule in the isomeres of the fundamental compounds, but the "chain-type" is dominant. In benzole and its derivatives we have a radical departure from this type in the "ring-type."

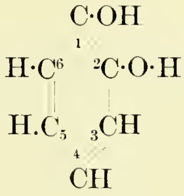
Benzole



Note that the four bonds of the carbon atoms are reciprocally satisfied as indicated, the particular location of the double bond being, of course, conventional. Note also that this hydrocarbon has a much larger proportion of carbon than is the case in the chain-type of hydrocarbons. The hydrogen atoms are displacable by monads or monad radicals, thus giving rise to a long series of *Benzole derivatives* or "Aromatic compounds." Phenol, Carbolic acid, Phenyl-hydroxide or hydroxy benzole has the following formula:



If two of the H's be displaced by hydroxyl the relative position of these two hydroxyls is not a matter of indifference; if they are adjacent to each other, thus:

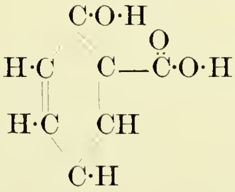


it is called *ortho*-dihydroxybenzole (*catechol*).

If the two hydroxyls are not adjacent, but occupy the positions 1·3 or 1·5 the compound is called *meta*-dihydroxybenzole (resorcinol). If the radicles are symmetrically opposite, as at position 1·4, the compound is a *para*-compound, in this case, *para*-dihydroxybenzole (quinol or hydroquinone).

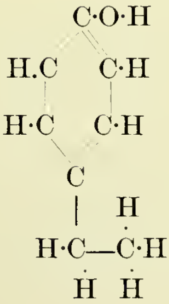
A few examples will show the general structure of the bodies.

(1) Orthohydroxy benzoic or salicylic acid



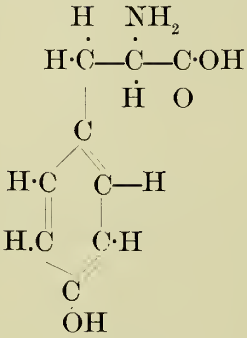
or $C_6H_4{\cdot}OH—COOH$.

(2) Para-ethyl-phenol or p-hydroxyphenyl ethyl:



or $C_6H_4{\cdot}OH—C_2H_5$

Para-hydroxyphenyl-*a*-amido-propionic acid or Tyrosin:



or $C_6H_4{\cdot}OH—CH_2—CHNH_2—COOH$.

2. THE CARBOHYDRATES.

a. Glycoses or Monsaccharids.

This most important class of organic compounds includes various *aldehydes*, *ketones* of the higher alcohols beginning with the triatomic propenyl alcohol or glycerol:
Glycerol + oxygen = water + glycerose,

$$2[CH_2OH — CHOH — CH_2OH] + O_2 =$$
$$2H_2O + \begin{cases} CH_2OH — CHOH — CHO, \text{ aldehyde of glycerol.} \\ CH_2OH — CO — CH_2OH, \text{ ketone of glycerol.} \end{cases}$$

The aldehydes in the carbohydrate series are called *Aldoses*, while the ketones are called *Ketoses*. Having three carbon atoms they are called *Trioses*. The glycoses include triosis, tetroses, pentroses, *hexoses*, heptoses, octoses and nonoses.

(*α*) *Trioses*,—Ex. *Glycerose* a mixed aldose and ketose ($C_3H_6O_3$).

(*β*) *Tetrose*,—Ex. *Erythrose* which is the aldose of erythrol, and has the formula:

$$CH_2OH—CHOH—CHOH—CHO; \text{ or } C_4H_8O_4.$$

(*γ*) *Pentose* —Ex. *Xylose* and *Arabinose* both having the formula ($C_5H_{10}O_5$).

(*δ*) *Hexoses* or *Glucoses* represent aldoses and ketoses of the hexatomic alcohols mannitol, dulcitol and sorbitol.

(I) *Dextrose*; d-glucose, grape-sugar, is the aldose of sorbitol: $CH_2OH—(CHOH)_4—CHO$, or $C_6H_{12}O_6$. Destrose is a sweet, crystalline substance, whose solutions rotate polarized light to the right, *i. e.*, dextro-rotary.

(II) *Levulose*, d-Fructose, Fruit-sugar, is the ketose of mannitol: $CH_2OH(CHOH)_3—CO—CH_2OH$. This sugar occurs in honey and in many fruits.

(III) *Galactose*, or d-galactose is the aldose of dulcitol.

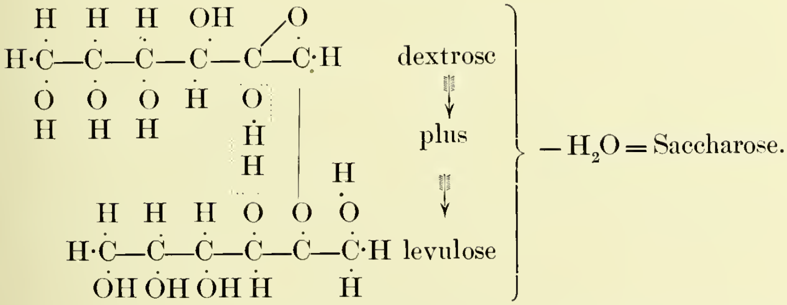
(IV) Mannose is the aldose of mannitol.

The hexoses or glucoses are incomparably more important than any of the other glycoses.

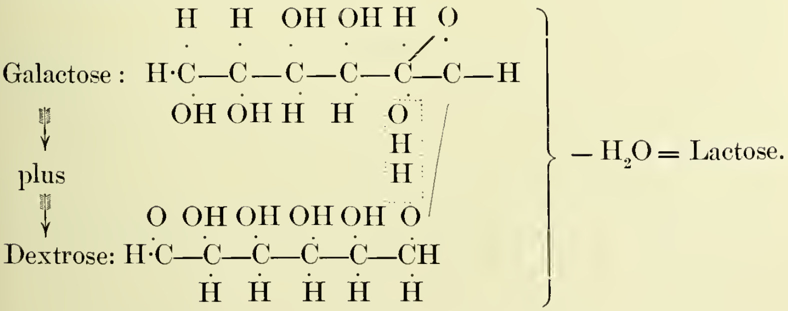
b. Sucroses or Disaccharids.

These are double-grouped sugars which represent a combination of two hexose groups minus a molecule of water. The following formula represents what takes place in the molecule in the formation of saccharose.

(*a*) SACCHAROSE OR CANE SUGAR.



(*b*) LACTOSE is likewise composed of a galactose group with a dextrose group dehydrated.



(*c*) MALTOSE is an end product of the action of amylolytic ferments upon starch, the hydrolysis of the starch molecule being effected before its cleavage into maltose and a dextrine. The dextrine is in turn subjected to hydrolytic cleavage resulting in maltose and another dextrine. The structure of the maltose molecule has not been sufficiently fully studied to present here. Its quantitative formula is $C_{12}H_{22}O_{11}$. In common with dextrine, lactose and fructose it reduces Fehling's solution.

c. The Polysaccharids or Amyloses.

To this class of carbohydrates belong the *starches, gums, dextrines* and *cellulose.* The molecular constitution is unknown. The members of the class have in common the general formula $(C_6H_{10}O_5)_n$. To the quantity n various values have been assigned.

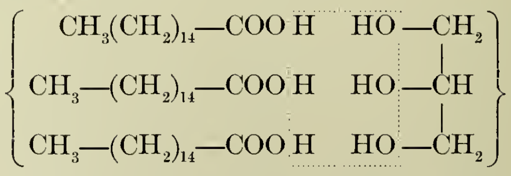
- Carbohydrates.
  - Monosaccharids, or Glycoses.
    - Trioses: Glycerose.
    - Tetroses: Erythrose.
    - Pentoses: Xylose, Arabinose.
    - Hexoses, or Glucoses.
      - Dextrose, or Grape-sugar.
      - Levulose, Fructose, or Fruit-sugar.
      - Galactose.
      - Mannose.
  - Disaccharids, or Sucroses.
    - Saccharose.
    - Lactose.
    - Maltose.
    - Isomaltose.
  - Polysacchnids, or Amyloses.
    - The Dextrines.
      - Amylo-Dextrine.
      - Erythro-Dextrine.
      - Achroödextrine α.
      - Achroödextrine β.
    - The Gums: Gum arabic, etc.
    - The Starches: Vegetable starch; glycogen.
    - Cellulose.

3. THE FATS.

In our review of the fundamental carbon compounds we have found a series of normal fatty acids which are derived from the monatomic alcohols. These fatty acids have the general structural formula:

$CH_3—(CH_2)_{n-3}—COOH$. The 16th member of this series is Palmitic acid, which has the formula $CH_3—(CH_2)_{14}—COOH$. Propenyl alcohol or glycerol is the first member of the series of triatomic alcohols and has the formula: $CH_2OH—CHOH—CH_2OH$ or $C_3H_5(OH)_3$.

When these two bodies are brought together under proper conditions there is a combination of one molecule of glycerol with three molecules of the fatty acid to form one molecule of *Palmitin* or *Tripalmitin,* one of the common fats:



$$\left\{\begin{array}{ll} CH_3(CH_2)_{14}—COO\,H & HO—CH_2 \\ & \qquad\;| \\ CH_3—(CH_2)_{14}—COO\,H & HO—CH \\ & \qquad\;| \\ CH_3—(CH_2)_{14}—COO\,H & HO—CH_2 \end{array}\right\}$$

$$=3H_2O+[CH_3—(CH_2)_{14}—COO]_3—C_3H_5.$$

3 Palmitic acid + glycerol = water + Palmitin or Tripalmitin.

In a similar way *Stearin* or *Tristearin* is formed from three molecules of stearic acid and glycerol, and has the formula: $[CH_3 — (CH_2)_{16} — COO]_3 — C_3H_5$.

Olein is a similar combination of three molecules of oleic acid (which is the 18th member of the oleic acid series, derived from the triatomic alcohols), and has the formula: $[CH_3 — (CH_2)_{14} — (CH)_2 — COO]_3 — C_3H_5$ or $(C_{18}H_{33}O_2)_3 — C_3H_5$. Palmitin, stearin and olein are the fats which are deposited in the adipose tissue of the animal body. Palmitin has a melting point of 45°C., stearin, 53°–66°C.; olein, 0°C. The animal fats are mixtures of these three constituents in various proportions peculiar to each species of animal.

The melting point of a mixture is the proportional average for the fats which compose the mixture. Both palmitin and stearin have a melting point above animal temperature. The fat of the animal body is always in a fluid state during life. The mixture of the three constituents must include sufficient olein to insure the fluidity of the fat at body temperature. But the melting point of the fat of different animals varies through a wider range than does the temperature of the animals. Certain of the chemical reactions of fats will be discussed in connection with their digestion and metabolism.

4. THE PROTEIDS.

The term proteids is a general one which includes a class of compounds of which egg-albumin, serum-albumin, hæmoglobin and fibrin may serve as examples. Though any of these may serve as animal food in common with the carbohydrates and the fats, they stand much nearer to living protoplasm than do carbohydrates and fats.

In fact the living matter which we call protoplasm and which possesses the marvelous power of liberating the energy which we call life, if deprived of life and subjected to chemical analysis, is shown to be only a mixture of proteids, together with various substances which may represent foodstuffs, in various stages of anabolism or cleavage products of protoplasm in various stages of katabolism. Just what changes take place between the departure of life and the resolution of the protoplasm into the various compounds just referred to, it is impossible to say. Of the various foodstuffs and katabolites found in protoplasm it is likely that all or nearly all are purely incidental to the life processes and that the matter which actually possesses life, *i. e.*, the true protoplasm, is a substance quite like the simple proteids chemically.

The chemistry of the proteids is still a collection of facts which fail to reveal the quantitative formula, much less the structure of the molecule. The most trustworthy analysis of egg-albumin is that of Franz Hofmeister (*Zeitsch. für physiol. Chemie*, Bd. 16, 1892) which resulted in the following formula:

Egg-albumin = $C_{204}H_{322}N_{52}O_{66}S_2$.

Though the molecular formula for egg-albumin may be modified by subsequent investigations it serves to indicate: (1) That typical proteids contain C, H, O, N, and S, (2) that typical proteids are made up of exceedingly large and complex molecules.

Besides the elements above enumerated some of the proteids (nucleo-proteids) contain *phosphorus* and some (chromo-proteids) contain *iron*.

The indiffusibility of most of the proteids may be due to the great size of the molecule.

The proteids are necessary constituents of animal foods. There is a certain minimum proteid requirement for every animal. If the food contain less than that the animal must die of malnutrition. On the other hand carbohydrates or fats or both of these may be withheld from an animal and no serious result will follow. The reasons for these facts will be given later. The facts are mentioned here to impress the student with the great importance of the proteids in nutrition.

Certain chemical characteristics of the proteids will be mentioned in connection with their classification.

CLASSIFICATION OF PROTEIDS.

a. Simple Proteids.

1. **Albumins.**—Soluble in water; and in a saturated solution of $MgSO_4$ or NaCl; insoluble in a saturated solution of $(NH_4)_2SO_4$. The albumins are coagulated by moderate heat, 63° to 75° C., and respond typically to the xanthoproteic test, Millon's reagent and other *general* proteid tests. The following native albumins may be given. (I) *Egg-albumin*, precipitated by ether (Halliburton). (II) *Serum-albumin*, not precipitated by ether (Halliburton). It is the principal proteid constituent of blood plasma. (III) *Lacto-albumin* is one of the proteid constituents of milk. When milk is boiled the lacto-albumin coagulates and collects upon the surface in a thin membrane. (IV) *Myo-albumin* is one of the proteids of muscle-tissue. (V) *Vegetable albumin*, of which there may be several kinds.

2. **Globulins.**—Insoluble in water, in saturated solutions of $MgSO_4$, NaCl, and $(NH_4)_2SO_4$; but soluble in dilute NaCl solution: (I) *Serum-globulin*, one of the proteids of blood-plasma and of lymph. (II) *Fibrinogen* is the plasma or lymph-proteid which is coagulated or precipitated under the influence of fibrin ferment and the calcium salts. The coagulated form probably somewhat modified chemically is called *fibrin*. (III) *Myosinogen*, the prin-

cipal proteid of living muscles. It coagulates after death and is in its modified form called *myosin*. (IV) *Myo-globulin*, associated with myosinogen in the composition of muscle-tissue. (V) *Globin*, one of the constituents of hæmoglobin. (VI) *Vegetable globulin*, there are probably several forms.

b. Combined Proteids.

1. **Nucleo-Proteids.**—These bodies are native compounds of nuclein with proteid. The nuclein contains phosphorus, hence all nucleo-proteids contain phosphorus, most of them contain iron. (I) *Casein*, the principal proteid of milk. In the non-coagulated condition it is usually called *caseinogen*. (II) *Vitellin*, the principal proteid of egg-yolk. (III) *Nuclein*, or *cell-nuclein*, the chief proteid of the nuclei of animal and vegetable cells.

2. **Chromo-Proteids** are native compounds of a proteid with an animal pigment: (I) *Hæmoglobin*, globin with hæmatin in a true chemical combination. The pigment is hæmatin which contains iron. (II) *Histo-hæmatin*, tissue hæmatin especially the hæmatin of muscle tissue, also called myo-hæmatin.

c. Derived Proteids.

To this class belong all of those modified proteids which are derived from native or combined proteids by physiological processes.

1. **Albuminates.**—These bodies are derived from the native proteids through the action of an acid or alkali. (I) *Acid-albumin*, formed in the stomach by the action of HCl or other acid upon albumin. *Syntonin* is a corresponding variation of myosin. (II) *Alkali-albumin*, formed in the small intestine by the action of the alkaline pancreatic juice upon the native proteids of the foods.

2. **Proteoses and Peptones.**—These substances are derived from native proteids, or from albuminates by hydrolysis, probably by a hydrolytic cleavage of proteids especially of the albuminate derivatives of native proteids.

d. Albuminoids.

These substances are closely related chemically to the other proteids and are derived from the native proteids by metabolic processes.

1. **Native Albuminoids.**—These include those albuminoids which exist normally in the animal body. (I) *Collagen*. The substance of which white fibrous connective tissue is composed. It is also a constituent of bone and of cartilage. (II) *Elastin*. The substance of which yellow, elastic fibers of connective tissue is formed. (III) *Mucin*. The chief constituent of the secretion

of mucous glands and an important constituent of the secretion of all of the digestive glands. It is a combination of a proteid with a carbohydrate and has been classified among the combined proteids as a glyco-proteid. (IV) *Keratin.* The horny material which is characteristic of the corneous layer of the epidermis, of nails, hair, horns, hoofs and feathers. Keratin has a much larger proportion of sulphur than other proteids have. *Neuro-keratin* is found in the medullary sheath of nerves.

2. **Derived Albuminoids.**—This class contains one example namely: (I) *Gelatin,* which is derived from *collagen* by hydration. It is an artificial product and is prepared by long boiling of any of the connective tissues of the animal body. The collagen at first insoluble, becomes hydrated and soluble gelatin, which on cooling sets into a jelly. When the excess of water evaporates the mass is amorphous and vitreous. It is soluble in hot water, indiffusible, gives most of the general proteid reaction and what is of great importance is *digestible.* It follows the general course of proteid digestion and is absorbed as gelatin-peptone. This gelatin-peptone can be katabolized in the tissues but it can not be built up into tissue protoplasm. Its importance in nutrition will be discussed under metabolism.

Protenoid Substances.

Enzymes.—The origin and the behavior of unorganized ferments leave little doubt that they are of the nature of proteids, perhaps typical proteids. Among the unorganized ferments may be mentioned: (I) Thrombin; (II) rennin; (III) ptyalin; (IV) pepsin; (V) trypsin; (VI) amylopsin; (VII) steapsin; (VIII) invertin.

5. FERMENTS AND ENZYMES.

a. Ferments in General.

Every living cell has the power to cause chemical reactions. Food materials are absorbed by the cell and are either first built up into protoplasm by a series of anabolic reactions, to be later subjected to a series of katabolic reactions, or directly subjected to katabolism. A tissue cell of a complex organism selects from the tissue plasma which surrounds the cell, the materials which are to enter the series of metabolic changes. A unicellular organism selects the materials from the liquid or other medium which immediately surrounds it. The materials so selected may be called the cell-foods. The foods selected by different one-celled organisms are as different as the heredity and environment of the organisms.

Whether or not the food must be built up into living protoplasm before it can be broken up into simpler bodies is still a matter of controversy. There is no doubt, however, that sooner or later all of the material absorbed by the living cell must be katabolized or broken up into simpler compounds.

After a certain number of katabolic changes the organism seems to have exhausted the energy of the material as far as it is capable of doing so. The final products of the katabolism (katabolites) are useless to the organism and are rejected (excreted). Among the katabolites are: CO_2, H_2O, NH_3, CH_4, H_2, H_2S.

These all represent compounds or elements whose energy is practically exhausted. There are many cell katabolites which are more or less complex and represent much energy: Sugar, Alcohol, Acetic Acid, Butyric, etc., etc.

Among the above mentioned katabolites are several which are gaseous. If these gaseous materials are given off in sufficient quantities they escape in bubbles. If the unicellular organism, *e. g.*, the yeast cell, is living in nutrient fluid containing sugar —dextrose—it will take up the sugar, and will excrete alcohol and CO_2. The CO_2 escapes in gaseous form. The observation of this phenomenon gave rise to the term FERMENTATION. The organism which causes the fermentation is called a FERMENT. In the light of the chapters on general or cellular physiology and of the introductory statements above it must be evident that *fermentation is a phase of cellular nutrition.* The term has been extended to include *all of those phases of the nutrition of unicellular organisms which involve the consumption of complex substances and the excretion of simpler ones.* The term *ferment* is applied to all the unicellular organisms which cause *fermentive* or *putrefactive* changes. As examples of these organisms one may enumerate: (I) The yeast plant, *Saccharomyces cerevisiæ*, which consumes sugar and excretes alcohol and CO_2. (II) The *Bacterium lactis* which consumes milk-sugar and water and excretes lactic acid ($C_{12}H_{22}O_{11} + H_2O = 4\,C_3H_6O_3$. (III) The *Mycodermi aceti*, which consumes alcohol and oxygen and excretes acetic acid ($C_2H_6O + O = H_2O + C_2H_4O_2$). (IV) Pasteur's *Fermentum butricum*, one of the vibriones, which consumes lactic acid, malic acid, tartaric acid, or mucic acid and excretes *butyric acid*, with a combination of various accompaniments (CO_2, H_2O, H_2, or acetic acid) according to the food consumed. (V) The *Vibrios* which consume proteid matter and produce in a liquid containing it what is known as *putrid fermentation* or *putrefaction.* Among the excreta may be enumerated: Leucin, tyrosin, formic, acetic, proprionic, butyric, valerianic, caproic and caprylic acids; ammonia, ethylamine, propylamine, trimethylamine, CO_2, H_2S, H and N.

All of the ferments enumerated above are micro-organisms; the saccharomyces being a unicellular fungus and the remaining examples being bacteria. These organisms, though perhaps less sensitive to variations in the supply of oxygen than most living things, nevertheless are much influenced in their activities by the presence of free oxygen. The subject was most exhaustively studied by Pasteur. Summing up his studies Pasteur said (Comp. Rend. de l' Acad. des Sci., Vol. 75, p. 784): "The weight of yeast which is produced under these conditions (*i. e.*, in the presence of free oxygen gas) during the decomposition of sugar increases progressively, and approaches the weight of the decomposed sugar, in exact proportion as its life goes on in the presence of increasing quantities of free oxygen gas.[1] Guided by these facts I have been gradually led to look upon fermentation as a necessary consequence of the manifestation of life when that life goes on without the direct combustion due to free oxygen. We may see as a consequence of this theory that *every organism, every cell which lives or continues its life without making use of atmospheric air, or which uses it in quantities insufficient for the whole of the phenomena of its own nutrition must possess the characteristics of a ferment with regard to the substance which is the source of its total or complemental heat.*"

Thus saccharomyces supplements the energy liberated through oxidation of its own tissues with free atmospheric oxygen, by energy liberated through katabolism of sugar. Some organisms, notably the vibriones, dispense with atmospheric oxygen altogether, carrying on all their life activities with the energy liberated through the katabolism of proteids.

b. **Enzymes.**

In our discussion of ferments we have mentioned only elementary unicellular organisms. In every case the organisms recognized as ferments live in a fluid or semifluid medium. Their pabulum is readily absorbable by the organism. We come now, however, to the consideration of Nature's method of adaptation to new conditions. In a grain of corn or barley the embryo plant is imbedded in a quantity of starch stored up by the parent plant for the nourishment of the germinating plantlet. Though the food supply surrounds the embryo it is an insoluble and unabsorbable solid.

How is it to be made soluble and absorbable? *The cells of the embryo secrete diastase which brings about the hydrolysis or hydrolytic cleavage of the starch molecules changing them to dextrose which is soluble and absorbable.* The plant kingdom abounds in similar examples. Diastase and similar substances are called ferments or

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[1] "In fermentation without oxygen, the ratio between the sugar decomposed, and the yeast formed, is from 60 or 80 to 1, while in fermentation in the presence of oxygen it is only 4 or 10 to 1."

Enzymes. It is not alive; it is not organized, and has, therefore, been called an *unorganized ferment.* The distinction between an organized and an unorganized ferment, or between a ferment organism and an enzyme, may be more apparent than real. It is most probable that the distinction is simply one of location of the reaction, *i. e.*, (I) *intra-cellular fermentation* caused by an enzyme upon absorbed substances; (II) *extra-cellular fermentation* caused by an enzyme upon unabsorbed, unabsorbable substances.

But animal cells produce enzymes also. When solid food is taken into the alimentary tract it may be insoluble and unabsorbable, as is the case, for example, with starch and lean meat. Unless these foods be rendered soluble they will be useless to the organism. *Specialized cells along the alimentary canal secrete enzymes which bring about the hydrolytic cleavage of the food-molecules changing them to forms which are soluble and absorbable.* The specialized cells in question do not absorb the products of fermentation (digestion). Other cells and specialized tissues absorb the nutriment which is distributed throughout the organism by still other organs and tissues. The cells which secreted the enzyme finally receive their sustenance from the common treasury —the blood.

Enzymes may be classified as follows:

1. **Amylolytic Enzymes.**—*Diastase, Ptyalin, Amylopsin,* which change starch to maltose or dextrose, dextrine being an intermediate substance. The ultimate change wrought in the starch may be summed up in the following equations: $(C_6H_{10}O_5)_n + nH_2O = nC_6H_{12}O_6$, dextrose or in the following equation:

$$(C_6H_{10}O_5)_n + \frac{n}{2}H_2O = \frac{n}{2}C_{12}H_{22}O_{11},$$

Starch + water = maltose.

The steps of this process have been studied by numerous investigators. Neumeister's results will be given later under salivary digestion. The steps of the process for ptyalin or amylopsin are probably, in a general way, typical of all enzyme action.

2. **Inverting Enzymes.**—The *Invertin* which the yeast plant secretes for splitting cane-sugar into dextrose and levulose may be cited as an example. A similar enzyme, secreted in the small intestine, changes cane-sugar and maltose to dextrose.

3. **Proteolytic Enzymes.**—The *Pepsin,* secreted in the stomach, and the *Trypsin,* secreted by the pancreas, represent this class. They act upon proteids, converting them into peptones through several intermediate steps.

4. **Fat-splitting Enzymes.**—An example of this is the *Steapsin* of the pancreatic juice. It acts upon fat causing each molecule to

take up three molecules of water and split into three molecules of fatty acid and one molecule of glycerine.

5. **Coagulating Enzymes.**—Such as *Rennin* and *Thrombin*, the first precipitating caseinogen as casein and the second precipitating fibrinogen as fibrin. Note the radical difference between the first four classes and the last class. The first four classes change insoluble substances to soluble ones; the fifth class changes soluble substances to insoluble ones.

c. Conditions of the Activity of Ferments and Enzymes.

(*a*) The Optimum Temperature is 35° C. to 40° C., while the maximum is below the boiling point, the enzymes being destroyed by boiling. The action of enzymes is progressively less as the temperature falls from the optimum, being completely suspended by a zero temperature.

(*b*) The Enzyme is not Quantitatively Involved in the Reaction which it causes. The quantitative relations between AgCl precipitated from a solution of chlorides by a certain amount of $AgNO_3$ is definite and unvarying. Time is not a factor in the amount of AgCl thrown down. An enzyme, however, can work a greater change in two hours than in one. The smaller the amount of enzyme the longer the time it will require to work a particular change. Just what part the enzyme plays in the reaction is unknown. If it enters into the reaction by being molecularly incorporated in certain stages of the process it is later disengaged in its original form and may repeat its hydrolytic change upon fresh molecules of the pabulum. This repetition is not without limit, however; the enzyme becomes exhausted after a while and is no longer able to excite the reaction.

(*c*) Another Condition of the Action of an enzyme which is of the greatest importance to the higher organism is the *inhibitory influence* of the *accumulation* of the *products* of *enzyme action*. When peptones have reached a certain degree of concentration they stop the further action of the enzymes until the product already formed is removed (by absorption), when the enzyme resumes activity. The pathogenic germs which often threaten human life are inhibited by the accumulation of their own excreta. If a modified form of this excretion be introduced into the organism in the early stages of the development of the micro-organism, its activity (virulence) can be much weakened or completely aborted. The whole system of serum therapy, for example, with antitoxin, etc., depends upon this fundamental principle.

E. FOODSTUFFS AND FOODS.

1. DEFINITIONS.

Gould defines *foodstuffs:* "The materials that may be employed for the purpose of nourishment and tissue-formation." The same lexicographer defines foods: "The substances ordinarily employed as aliments." This distinction is not as clear-cut in the definitions as it is in use. The term foodstuff is employed as a generic term including all of those chemical compounds, "proximate principles of the older physiologists," which may be employed for the nourishment, growth and repair, of the organism.

Examples: Starch, sugar, fat, albumin.

A *food* is an article of diet which may be composed of one or more foodstuffs: Bread, composed of starch, glutin, fat, inorganic salts, water, etc., etc. *Beefsteak*, composed of various proteids, fats, inorganic salts, water, etc.; *Potatoes*, composed of starch, proteid, salts, cellulose, and water.

2. CHEMICAL COMPOSITION OF MILK AND OF THE ANIMAL BODY.

How shall we obtain a comprehensive idea of foods and foodstuffs? Nature furnishes every young mammal with a food—milk—which most perfectly satisfies the requirements enumerated above, growth and repair, and whose analysis may give us a clue to the chemical characters that foodstuffs should possess:

Chemical analysis of milk.	Water						87. %
	Solids.	Organic.	Proteids.	Caseinogen. Lact-albumin.			4. %
			Fats.	Olein,	.43	*100 parts.*	4. %
				Palmitin,	.33		
				Stearin,	.16		
				Butyrin, Caprioin, Caprilin,	.07		
			Carbohydrates—Lactose.				4.4%
		Inorganic:—$CaHPO_4$, $CaCO_3$, $NaCl$, $MgCl_2$, etc.					0.6%

When we compare the chemical constituents of the mammalian body with the chemical composition of that food—milk—which nature furnishes to young mammals, we find an exact correspondence in the general constituents, *i. e.*, each contains water in large proportion, proteids, fats, carbohydrates and salts, composed largely of phosphates, chlorides and carbonates. The most noticeable difference between the two lists is the great variety of proteids in the mammalian body, while there are only two or three varieties in milk. If, of a family of young mammals, a part be sacrificed to chemical analysis at birth and the rest after their period of growth on a milk diet, the results of the analysis will be practically identical qualitatively, but all of the constituents will be found much greater in quantity in those which have had the milk diet. Such an experiment demonstrates conclusively that out of a few kinds of proteids many kinds may be built up.

The following table giving the chemical constituents of the animal body will show what the carnivorous animal eats.

Chemical Composition of the Animal Body.	Water				about 67 %
	Solids.	Organic.	Proteids.	Albumins.	Serum Albumin. Myo-albumin.
				Globulins.	Serum Globulin. Fibrinogen. Myosin. Myo-globulin. Globin. Crystallin.
				Nucleo-Proteids:	Nuclein.
				Chromo-Proteids.	Hæmoglobin. Histo-Hæmatin.
				Albuminoids.	Collagen. Elastin. Mucin. Keratin.
				Enzymes.	Thrombin. Rennin. Ptyalin. Pepsin. Trypsin. Amylopsin. Steapsin. Invertin.
			Fats.	Palmitin. Stearin. Olein, etc.	
			Carbo-hydrates.	Glycoses :—Dextrose. Saccharoses :—Lactose, during lactation. Amyloses :—Glycogen.	
		Inorganic.	$NaCl$, $CaHPO_4$, $CaCO_3$ KCl, $Ca_3(PO_4)_2$, Na_2CO_3 $MgCl_2$, Na_2HPO_4, $NaHCO_3$ $CaCl_2$, NaH_2PO_4.		Fe in organic combination in hæmatin and tissues in general.

As the next step in our discussion let us make a list of those ingested by a carnivorous animal. The wolf or fox catches and eats rabbits or birds. This food of the carnivorous animal has already been analyzed and we see that it corresponds in every respect to the body which it must nourish. Our first and most natural thought is that the proteids of the rabbit become the proteids of the wolf, kind for kind, *i. e.*, the myosin or muscle-proteid of the rabbit becomes the muscle-proteid of the wolf. But this natural inference is fallacious. All proteids are, during digestion, reduced to peptones from which, after absorption into the circulatory system, the various proteids of the carnivorous animals are built up. If there be an excess of proteid in the blood this excess may be deposited in the changed form of fat. Further, the quality and quantity of fat in the wolf does not correspond to the quality and quantity of this constituent in the rabbit. The only inference possible is that the rabbit fat, after being taken up into the blood of the wolf, is partially consumed in some metabolic process and partially deposited, but the several constituents—olein, palmatin and stearin—are deposited in a new proportion peculiar to the wolf. Similar observations and conclusions might be made regarding the carbohydrates. But where does the rabbit obtain this ample list of constituents? He does not get his food so nearly prepared as does the fox. He eats only herbaceous material—he is herbivorous. His diet of barks, vegetables and tender herbaceous shoots, if subjected to chemical analysis, will be found to contain, besides water, very large quantities of carbohydrates and very small quantities of fats and proteids. Among the carbohydrates the principal constituent is cellulose, though there is also a small quantity of glucose and starch. The wolf is quite unable to accomplish the first step in the digestion of cellulose.

3. CLASSIFICATION OF FOODSTUFFS.

- Foodstuffs.
  - Inorganic.
    - Water.
    - Salts.
      - NaCl, KCl.
      - $Na_2CO_3K_2CO_3$, $MgCO_3$.
      - Na_2SO_4, K_2SO_4, $MgSO_4$.
      - Na_2HPO_4, K_2HPO_4, $MgHPO_4$, $CaHPO_4$.
      - Na, K, Ca, etc., combined with fruit acids: (Tartaric, citric, malic, etc).
      - Fe combined with animal proteids (Hæmoglobin) and with vegetable compounds (Chlorophyll).
  - Organic.
    - Carbohydrates.
      - Amyloses
        - Starch.
        - Glycogen.
        - Cellulose.
      - Saccharoses.
        - Cane Sugar.
        - Lactose.
        - Maltose.
      - Glycoses.
        - Dextrose.
        - Levulose.
        - Galactose.
    - Fats.
      - Palmitin.
      - Stearin.
      - Olein.
    - Proteids.
      - Albumins.
      - Globulins.
      - Nucleo-Proteids.
        - Animal and vegetable varieties.
      - Chromo-Proteids.
      - Albuminoids, Collagen, etc.
      - Derived Albuminoid-Gelatin.

4. FOODS.[1]

I. INORGANIC FOODS.

a. Water.

Water comprises between 67 per cent. and 70 per cent. of the mammalian body. It is a general solvent and diluent. All of the secretions of the body are composed very largely of water. It is an absolutely indispensable food. An adult requires from 2000 c.c. to 2500 c.c. every 24 hours. Of this about $\frac{1}{3}$ is taken in the form of liquid food (soup and beverages), leaving about 600 c.c. to 800 c.c. (3 to 4 glasses) per day to be taken as "drinking water." Many people take much less water than this. "One of the most universal dietetic failings is neglect to take enough water into the system." (Thompson.)

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[1] In the preparation of this section I have drawn freely upon Dr. W. Gilman Thompson's admirable work on *Practical Dietetics.* (D. A. & Co., 1893.)

One of the most important uses of water is as a *thermolytic* agent, regulating the body temperature through distributing the body heat, and through liberating heat from the surface of the body by evaporation of perspiration.

Beverages are drinks which represent aqueous solutions or dilutions of various organic, usually vegetable products: tea, coffee, cocoa, chocolate, lemonade, and allied drinks, cider, beer, ale, wine, brandy, etc. They serve to *relieve thirst*, as *nutrients*, as *diuretics*, as *diaphoretics*, as *diluents*, as *demulcents*, as *tonics*, as *stimulants*, as *intoxicants*.

Some of these offices are necessary, some are permissible, while some are not, from a physiological standpoint, permissible.

b. **Salts.**

Salts in general serve the following uses in the system:

1. "To regulate the specific gravity of the blood and other fluids of the body."

2. "To regulate the chemical reaction of the blood and the various secretions and excretions."

3. "To preserve the tissues from disorganization and putrefaction."

4. "To control the rate of absorption by osmosis."

5. "To enter into the permanent composition of certain structures, especially the bones and teeth."

6. "To enable the blood to hold certain materials in solution."

7. "To serve special purposes, such, for example, as the influence of sodium chloride on the formation of hydrochloric acid, and that of lime salts in favoring coagulation of the blood."—(W. G. T.)

As a rule, little care need be given to the salts, because the vegetable and animal foods of a mixed diet all contain salts, making, when taken together, a list sufficient in quantity and quality, with the single exception of the sodium salts. Plants are especially rich in potassium salts and comparatively poor in sodium; thus herbivorous animals need more of the sodium salts, especially sodium chloride, than appears in the vegetable diet, and to this end eat earths rich in these salts—thus have been established the "deer-licks," visited by the herbivora of a whole region.

Carnivora seem to get a sufficient supply of the salts from the flesh of the herbivora which they consume. Omnivora need supplementary sodium salts in proportion to the part which vegetables play in their diet. Vegetarians need extra sodium chloride. Certain disturbances of nutrition (anæmia, rachitis, etc.) arise from or result in a deficiency of certain minerals or mineral salts. A serious problem confronting the clinicians has been to determine the form of mineral nutriment best adapted to the animal organism suffering from malnutrition. Whether the needed salts should be given directly as such, or whether vegetable and animal foods rich in the needed salts should be made predominant in the diet, are the alternatives between which the clinicians wavered for many years. The general consensus of opinion, as expressed in practice, is in favor of the second alternative. Patients who need more iron are given eggs, lean meats, cereals, peas, beans and "greens" rich in chlorophyll. Patients who need bone-making salts are given, among other foods, an abundance of milk, which contains calcium salts in a form and proportion which seem best adapted to the system.

II. ORGANIC FOODS.

§*A*. VEGETABLE FOODS.

In these bodies the carbohydrates predominate. The following table of analysis by Dr. C. E. Woodruff, Asst. Surgeon U. S. Army, gives vegetable foods with the constituent foodstuffs and energy represented:

FOOD.	WATER.	PROTEIDS.	FATS.	CARBO-HYDRATES.	SALTS.	ENERGY IN KILO-CALORIES PER LB.
Sugar	2.0%	—	—	97.8%	0.2%	1820 Calories
Syrup	43.7	—	—	55.0	2.3	1023 "
Tapioca Cornstarch	2.0	—	—	97.8	0.2	1820 "
Rice	12.4	7.4	0.4	79.4	0.4	1630 "
Macaroni	13.1	9.0	0.3	76.8	0.8	1406 "
Flour	12.5	11.0	1.0	74.9	0.5	1644 "
Cornmeal	15.0	9.2	3.8	70.6	1.4	1645 "
Oatmeal	7.6	15.1	7.1	68.2	2.0	1850 "
Beans or peas	12.6	23.1	2.0	59.2	3.1	1615 "
Potatoes	78.9	2.1	0.1	17.9	1.0	375 "
Onions	87.6	1.4	0.3	10.1	0.6	225 "
Cabbage	92.0	2.1	0.6	5.5	1.1	155 "

a. **Sugars.**

This general sub-class of the carbohydrate foodstuffs has the great advantage that it requires little or no digestion, may be directly absorbed and very readily assimilated. The most common food-sugars are: Cane-sugar, glucose, and milk-sugar. Cane-sugar or saccharose is derived from the sap of sugar-cane, beet-roots, and maple trees. Glucose or dextrose is manufactured from starch, makes a prominent constituent of powdered sugar and is used in the table syrups. It is the most common fruit and vegetable sugar; in grapes, cherries, figs, dates, bananas, onions, turnips, cabbage, etc.

Milk-sugar or lactose constitutes about 4 per cent. of cows' milk and is usually used only in milk. Honey is a natural syrup formed by flowers and collected by bees. König's analysis gives: Water, 16.13 per cent.; fructose, 78.74 per cent.; saccharose, 2.69 per cent.; nitrogenous matter, 1.29 per cent.; salts, 0.12 per cent.

b. **Foods in which Starch Predominates.**

1. **Cereals.**—These comprise grains including wheat, corn, rice, rye, oats, barley. The cereals with potatoes form the most common source of starch. The cereals are usually used in the form of meal or flour. Not only do the cereals contain considerable proteids with some fats, but in the preparation of these meals and flours for eating it is customary to make important additions in the form of milk, eggs and fat so that the resulting preparation is a complex food which generally represents all of the foodstuffs in a proportion approaching that of a typical diet.

The following table illustrates this as far as it concerns bread and crackers.

COMPOSITION OF BREADS AND CRACKERS (Clark quoted by Thompson).

FOOD.	WATER.	NUTRIENTS.	PROTEIDS.	FATS.	CARBO-HYDRATES.	SALTS.
Wheat bread.	32.5%	67.5%	8.8%	1.9 %	55.8%	1.0%
Graham bread.	34.2	65.8	9.5	1.4	53.3	1.6
Rye bread.	30.0	70.0	8.4	0.5	59.7	1.4
Soda Crackers.	8.0	92.0	10.3	9.4	70.5	1.8
Grabam "	5.0	95.0	9.8	13.5	69.7	2.0
Oatmeal "	4.9	95.1	10.4	13.7	69.6	1.4
Oyster "	3.8	96.2	11.3	4.8	77.5	2.6
Graham bread nutrients.		100%	14.8	22.2	83.7	To compare the nutrients of graham bread with a typical diet.
Typical diet nutriment.		100%	17.5	8.4	73.8	

2. **Other Starchy Foods.**—Tapioca and arrow-root are prepared from the root-stalks of certain tropical and subtropical plants. Sago is extracted from the pith of certain tropical palms. Tapioca and sago are practically pure starch, while arrow-root contains H_2O 15.4 per cent., proteids 0.8 per cent., and starch 83.3 per cent.

3. **Legumes.**—Beans and peas contain, besides a large amount of starch, so large a proportion of proteids that they may be used

as one of the recognized sources of proteids, though the animal foods form the most important source of proteids.

4. **Roots and Tubers.**—White potatoes, sweet potatoes, beets, carrots, parsnips, turnips, radishes, etc., represent this class of vegetable foods. All of this class are rich in salts, especially the salts of potassium. The nutrient portion of potatoes consists largely of starch; while in the other vegetables enumerated it consists chiefly of sugar.

The following table, combined from analyses by Letheby and by König, gives the nutrient values of the

Roots and Tubers.

Foods.	Water.	Proteids.	Fats.	Sugar.	Starch.	Cellulose.	Salts.	Analyst.
Potato (white).	75.0%	2.10%	0.2 %	3.2	18.8	.... ..	0.7	Letheby
Potato (sweet).	67.5	1.5	0.3	10.2	16.0	0.45	2.6	Payen
Parsnips.	82.0	1.1	0.5	5.8	9.6	....	1.0	Letheby
Carrots.	83.0	1.3	0.2	....	8.4	....	1.0	"
Onions.	86.0	1.86	0.1	2.8	No starch "extractives" 8 %	0.7	0.7	König
Beet-root.	87.1	1.4	.....	0.6	....	1.0	0.9	"
Turnips.	91.2	1.0	0.2	4.1	"Extractives" 1.9	0.9	0.75	"

All of the foods in the above table are preserved for use in winter, during which season the absence of green vegetables makes them especially desirable and palatable.

5. **Green Vegetables.**—These are used mostly "*in season.*" They represent very little nutriment but serve rather to sharpen the appetite for heavier foods. Spinach is rich in iron and is an especially fine food for use when more iron should be introduced into the system.

Lettuce and celery both act as sedatives on the nervous system. Rhubarb has a laxative action, while asparagus acts as a diuretic. The following table gives analysis of a few of the more important green vegetables.

Composition of Green Vegetables (König, quoted by W. G. T.).

Food.	Water.	Proteids.	Fats.	Sugar.	Extraction.	Cellulose.	Salts.
Celery.	84.1	1.5	0.4	0.8	11.0	1.4	0.8
Cabbage.	90.0	1.9	0.2	2.3	25.8	1.8	1.23
Cauliflower.	90.4	2.5	0.4	1.3	23.7	0.9	0.8
Spinach.	90.3	3.2	0.5	0.1	23.3	0.8	1.94
Asparagus.	93.3	2.0	0.3	0.4	22.3	1.1	0.5
Lettuce.	94.3	1.4	0.3	....	21.9	0.7	1.0

To this same class belong cucumbers, egg-plant, pumpkin, squash, and vegetable marrow.

6. **Fruits.**—The following table gives the composition of the principal fruits used in this country:

FRUITS.

FRUIT.	WATER.	NITROGENOUS MATTER.	SUGAR.	FREE ACIDS.		OTHER NON-NITROGENOUS MATTER.	CELLULOSE AND KERNEL.	SALTS.	ANALYST.
Apple.	83.6 %	0.4	7.7	0.8		5.2	2.0	0.3	Bauer.
Pear.	83.0	0.36	8.26	0.2		3.54	4.3	0.3	"
Peach.	83.0	0.65	4.5	0.9		7.2	6.06	0.7	"
Grape.	78.2	0.6	14.36	0.8		1.96	3.6	0.5	"
Strawberry.	87.66	1.1	6.3	0.9		0.5	2.3	0.8	"
Currant.	84.8	0.5	6.4	2.15		0.9	4.6	0.7	"
Orange pulp.	89.0	0.7	4.6	2.44		0.9	1.8	0.5	"
				FAT.					
Cherry.	49.9	2.1	32.2	0.3		14.3	0.6	1.6	Yeo.
Raisin.	32.0	2.4	57.26	0.5		7.5	1.7	1.2	"
				FAT.	ACID.				
Fig.	31.2	4.0	49.8	1.44	1.2	4.5	5.0	2.86	"

Thompson gives the following list of uses for fruits:

(*a*) "TO FURNISH NUTRIMENT."—The nutriment is chiefly found in the sugar. The most nutritious fruits are: fig, prune, grape, date, banana, cherry.

(*b*) "TO CONVEY WATER TO THE SYSTEM AND RELIEVE THIRST."—Besides melons, the orange, lemon, grape, and pear seem best adapted to this purpose.

(*c*) "TO INTRODUCE VARIOUS SALTS AND ORGANIC ACIDS WHICH IMPROVE THE QUALITY OF THE BLOOD AND REACT FAVORABLY UPON THE SECRETION."—The salts of especial importance are citrate, tartrate and malate of sodium and potassium. Citric acid and the citrates predominate in lemons and oranges; tartaric acid and the tartrates in grapes, and malic acid and the malates in apples, pears, peaches, apricots, gooseberries, currants (and rhubarb). The alkalinity of the blood and secretions is increased with a fruit diet, owing to the release of the K and Na from the organic acids and their combination as carbonates, phosphates, etc.

(The tomato is really a fruit, though in the diet it is associated with the green vegetables. It contains oxalic acid, which is injurious in uric acid diathesis.)

(*d*) TO SERVE AS THERAPEUTIC AGENTS.—(I) "*As anti-*

scorbutics; (II) *as diuretics;* (III) *as laxatives and cathartics."* The antiscorbutic action of such fruits as apples, lemons and oranges is due to their abundance of the salts of potassium, magnesium and calcium. The diuretic action of fruits is due in part to the water which they contain. The citrates which oranges and lemons contain are especially stimulating to the action of the kidneys. The laxative action of fruits is best marked in apples, figs, prunes, dates, grapes, peaches and berries.

(*e*) Fruits "STIMULATE THE APPETITE, IMPROVE DIGESTION, AND GIVE VARIETY TO THE DIET." (Quotations from G. W. Thompson.)

§ *B.* FATS AND OILS.

These important foods are found both in the vegetable and in the animal kingdom and may be considered here. Twenty per cent. of the normal body weight consists of fat. This is in small part derived directly from the fat of the food, but rather from the sugars and starches, with a small portion from the proteids. Most of the ingested fat is oxidized at once and supplies a considerable part of the animal heat. One may thus summarize the uses of the fats. The ingested fats serve:

(*a*) "TO FURNISH ENERGY FOR THE DEVELOPMENT OF HEAT."

(*b*) "TO SPARE THE TISSUES FROM DISINTEGRATION, for although their combustion in the body results largely in the production of heat, they also take part to some extent in tissue formation."

The deposited fats serve:

(*c*) "TO STORE ENERGY IN POTENTIAL FORM."

(*d*) "THROUGH THE SUBCUTANEOUS COAT OF ADIPOSE tissue, to conserve the heat of the body."

(*e*) "TO LUBRICATE and make more plastic various structures of the body and give rotundity to the form." (Quotations from W. G. T.)

The most important vegetable oils are: *Olive oil*, cotton-seed oil, used in dressings and cooking, and the oil of nuts.

Animal fats and oils are: Butter, cream, suet, lard, and the fats of beef, mutton, pork and fish. The yolk of eggs is also rich in oil.

§ *C.* ANIMAL FOODS, IN WHICH THE PROTEIDS PREDOMINATE.

The animal foods present a much less extensive variety than do the vegetable foods. The most important animal food is that one which nature prepares for all young mammals, viz., *milk*.

a. Milk.

One analysis of cow's milk (Bunge's) was given at the head of this section.

The following table gives the analysis of cow's milk and human milk by A. H. Leeds. (Quoted from W. G. Thompson.)

	"SOUND DAIRY MILK."	HUMAN MILK.
Reaction.	Faintly acid.	Alkaline.
Specific gravity.	1029.7	1031.3
Bacteria.	Always present.	Absent.
Fats.	3.75	4.13
Lactose.	4.42	7.0
Proteids.	3.76	2.0
Salts.	0.68	0.2
Total Solids.	12.61 %	13.33 %
Water.	87.39 %	86.67 %

Thompson enumerates the following as "the more important uses of milk":

1. **Purely as Food**: (*a*) "AS INFANT FOOD."

(*b*) "AS A FOOD FOR ADULTS."

(*c*) "AS A SOURCE of special food products and derivatives such as cream, butter, cheese, buttermilk, koumiss."

(*d*) "AS A MOST IMPORTANT CONSTITUENT in various composite foods, as bread, omelet, etc."

(*e*) AS A VEHICLE for the administration of other foods for invalids, *e. g.*, egg-albumin, beef meal, cocoa, meat juice, peptonoids, etc., etc.

2. **Therapeutic Uses of Milk**: (*f*) "AS A DIURETIC."

(*g*) "FOR ITS SOOTHING EFFECT on diseased mucous membranes of the alimentary canal."

(*h*) "TO LOOSEN A COUGH (when given hot)."

(*j*) "FOR RECTAL INJECTION," really a food in this case.

(*k*) "AS A VEHICLE for the administration of medicines. The following table gives the constituents of the more important derivatives of milk."

FOOD.	WATER.	PROTEID.	FAT.	SUGAR.	SALTS.	ANALYST.
Milk.	86.8	4.	3.7	4.8	0.7	Parkes.
Skimmed milk.	88.	4.	1.8	5.4	0.8	"
Cream.	66.	2.7	26.7	2.8	1.8	"
Cheese.	36.8	33.5	24.3	——	5.4	"
Butter.	6.0	0.3	91.0	——	2.7	"

b. Eggs.

Milk is nature's food for young mammals, and eggs are nature's food for young birds. Both of these natural foods contain all of the foodstuffs necessary for a developing animal. Bauer gives the average weight of the hen's egg as 50 grammes, of which the shell represents 7 gms. or 14 per cent., the white 27 gms. or 54 per cent., and the yolk 16 gms. or 32 per cent. Parkes allows only 10 per cent. of the weight for the shell, the yolk and white together being composed of: Water, 73.5 per cent.; proteids, 13.5; fats, 11.6; and salts, 1 per cent.

Eggs represent a concentrated diet, and though they contain considerable fat they are classed as a *proteid food.* Egg-albumin digests more easily in the natural uncooked state than when coagulated by cooking. Raw eggs are, however, quite unpalatable to most people and it is customary to cook them. Egg-albumin begins coagulation at 56.5° C. (about 134° F.) and the process progresses to about 70° C. (or 160° F.). If the temperature is raised to the boiling point the albumin becomes very densely coagulated and difficult of digestion. The most prevalent method of eating eggs is in various milk compounds: omelet, scrambled, custards, etc., etc.

This mixing of the egg with milk seems to correct the difficulty of indigestible coagula, besides making a most palatable food.

c. **Meats.**

We generally rely upon the lean meat of various animals for our supply of proteids, though it must not be forgotten that many of the cereals and the legumes contain a very large proportion of proteids; a proportion quite sufficient to insure the proper nutrition of the body without resort to the addition of lean meats. The variety which is given by the addition of meats to the diet would justify it, however, even if there were no other reasons favorable to it. Liebig said, "It is certain that three men, one of whom has had a full meal of meat and bread, the second cheese or salt fish (and bread), and the third potatoes, regard a difficulty which presents itself from entirely different points of view." The aggressive peoples of northern Europe and the western continent are the meat-eating people of the world. Besides overcoming the very great difficulties of a northern climate they have outstripped their vegetarian competitors in almost every field of human endeavor. Just what gives to a meat diet this subtle influence is a problem. That the influence exists is not a matter of controversy. In its extremes we see the difference in meat and vegetable diet wrought upon the lion and the ox; the vegetarian, though strong, is slow, clumsy and lazy; the meat-eater quick, graceful and alert.

The author does not wish to be understood to approve of an exclusively meat diet. Man is omnivorous. If meat makes too great a proportion of his diet disturbances of nutrition are almost sure to manifest themselves.

The fact is, Americans and Englishmen eat rather too much meat already.

We need meat, but we do not need it in immoderate quantities.

The following table gives the composition of some of the more common meats (including fish and "shell-fish").

FOOD.	WATER.	PROTEIDS.	FAT.	CARBO-HYDRATES.	SALTS.	ANALYST.
Beefsteak.	74.4	20.5	3.5	——	1.6	Parkes.
Fat beef.	51.	14.8	29.8	——	4.4	Pavy.
Lean beef.	72.	19.3	3.6	——	5.1	"
Fat mutton.	53.	12.4	31.1	——	3.5	"
Lean mutton.	72	18.3	4.9	——	4.8	"
Veal.	63	16.5	15.8	——	4.7	"
Fat pork.	39	9.8	48.9	——	2.9	"
Bacon.	15	8.8	73.3	——	2.9	"
Smoked ham.	27.0	34.0	36.0	——	10.0	Parkes.
Calves' liver.	72.3	20.1	5.6	——	1.5	Payen.
Poultry.	74.	21.	3.8	——	1.2	Parkes.
White fish.	78.	18.	2.9	——	1.	Parkes.
Canned salmon.	63.6	21.6	13.4	——	1.4	Woodford.
Crabs.	84.	15.	1.0	——	?.	"
Oysters.	87.	6.	1.2	3.7	2.	"

5. PREPARATION OF FOODS.

Thompson says that, "it is owing to the practice of cookery that the dietary of civilized man has been so much enlarged, and that it covers a wider range of materials than that which serves for the nourishment of lower animals."

The cooking of food serves the following purposes: (I) To render the organized structure of such foods as meats and vegetables more tender, therefore, more easy to masticate and to digest. (II) To render the foods more palatable through the flavors developed in cooking. Important as this is to those who have been used to cooked foods it is easy to see that it might be quite unimportant to the savage; the Eskimo, for example, seems to prefer his meat raw. (III) To kill any parasites and germs which may be in the food as received from the market.

The cooking is accomplished in the following general ways: (I) boiling, (II) stewing, (III) steaming, (IV) frying, (V) baking, (VI) roasting and broiling.

In *boiling* and *stewing* the cooking is conducted by a temperature which does not exceed 100° C. (212° F.). The two processes differ in this way: the food to be boiled is *plunged into boiling water*, this coagulates or hardens the surface, thus retaining within the mass the juices; the food to be stewed is put into cold water and the whole brought gradually to a boiling temperature, this process tends to extract the juices and to macerate the tissues somewhat. During the period of cooking which follows the above-described preliminary the two processes consist alike in keeping the temperature at 100° C. In *steaming* the food is subjected to the steam which escapes from water boiling in an unsealed receptacle. The steam does nor exceed 100° C. The effect is quite like that of boiling.

In *frying* the heat is transmitted to the food through the medium of heated fat or oil. Fats used in cooking may be heated to 400° F. before they begin to smoke. The food cooks therefore much more rapidly with this process than with those above described. The fat may sear the outside of the food or may permeate it to a greater or less extent. In any case the digestibility is somewhat decreased, in some cases it may be very much so.

In *baking*, *roasting*, and *broiling* the heat, as it radiates from coals or from stone or metal surfaces, is applied direct to the food. The temperature may thus be much higher than that of boiling water.

In a general way it may be said: (I) That all foods that are cooked at all should be kept at 100° C. long enough to destroy parasites and bacteria. (II) That eggs, unless incorporated as constituents in composite foods, should be cooked as little as possible, the less the better. (III) That starchy foods should be very thoroughly cooked. (IV) That meats in general should be cooked just long enough to develop the flavors most agreeable to the recipient.

DIGESTION.

A. SALIVARY DIGESTION.

1. THE SALIVA.
    - *a.* The Secretion of Saliva.
    - *b.* The Composition of Saliva.
2. THE CHEMISTRY OF SALIVARY DIGESTION.
3. FACTORS WHICH INFLUENCE SALIVARY DIGESTION.
4. MASTICATION.
5. DEGLUTITION.

B. GASTRIC DIGESTION.

1. THE GASTRIC JUICE.
    - *a.* The Secretion of Gastric Juice.
    - *b.* The Composition of Gastric Juice.
2. THE CHEMISTRY OF GASTRIC DIGESTION.
3. FACTORS WHICH INFLUENCE GASTRIC DIGESTION.
4. THE MOVEMENTS OF THE STOMACH.
5. VOMITING.

C. INTESTINAL DIGESTION.

1. THE DIGESTIVE FLUIDS OF THE INTESTINE.
    - *a.* The Secretion of Pancreatic Juice.
    - *b.* The Composition of Pancreatic Juice.
    - *c.* The Composition of the Bile.
2. THE CHEMISTRY OF INTESTINAL DIGESTION.
    - *a.* The Action of the Pancreatic Juice.
    - *b.* The Action of The Bile.
    - *c.* The Action of the Succus Entericus.
    - *d.* The Digestion of Milk: A Summary.
3. THE FACTORS WHICH INFLUENCE INTESTINAL DIGESTION.
    - *a.* The Influence of Bacteria.
    - *b.* The Influence of Cellulose.
4. THE REMNANTS OF INTESTINAL DIGESTION: FÆCES.
5. THE MOVEMENTS OF THE INTESTINES.
6. DEFECATION.

DIGESTION.

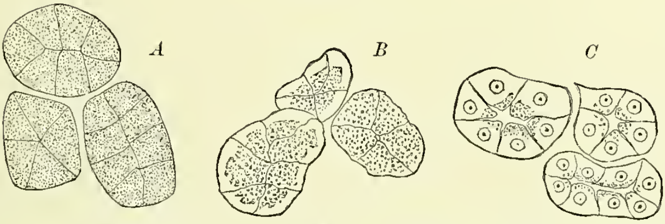
A. SALIVARY DIGESTION.

1. THE SALIVA.

a. The Secretion of Saliva.

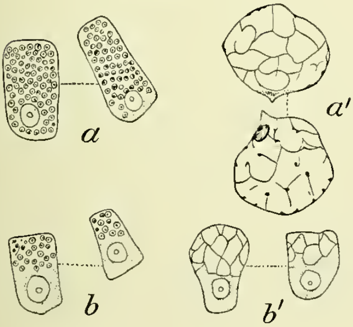
The term *saliva* is applied to the fluid secreted into the oral cavity. There are three principal pairs of glands whose secretion forms a part of the saliva: the *parotids*, the *submaxillary*, and the *sublingual*. Besides these six glands there are innumerable smaller mucous glands whose secretion serves only to moisten the surfaces of the membrane while the secretion of the salivary glands proper serves especially to moisten the food during mastication and to add to it a digestive ferment. These glands may be divided into two

FIG. 168.



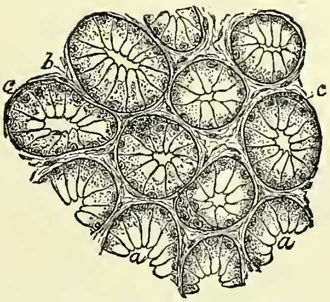
Alveoli of a serous gland-parotid. *A*, at rest; *B*, after a short period of activity; *C*, after a prolonged period of activity. In *A* and *B* the nuclei are obscured by the granules of zymogen. (SCHAEFER.)

FIG. 169.



Mucous cells from fresh submaxillary glands of the dog. *a*, from a resting or loaded gland; *b*, from a gland which has been secreting for some time; *a′*, *b′* similar cells which have been treated with dilute acid. (SCHAEFER.)

FIG. 170.



Mucous acini of human lingual gland: the secreting cells (*a*), being loaded with the slightly-staining secretion, appear clear and transparent; *c*, *c*, crescentic masses of granular cells—the demi-lunes of Heidenhain; *b*, interacinous connective tissue. (After PIERSOL.)

classes on the basis of the morphological changes which the cells of the glands undergo during the period of rest and activity. Fig. 168 shows the cells of serous glands, the parotid, while Fig. 169 shows the cells of a mucous gland, the submaxillary. Note that the cells of the serous parotid gland are subspherical and nearly fill the alveolus, leaving a narrow inter-cellular cleft which widens into a definite lumen when the cells are depleted by secretion. The nucleus is located in the center of the cell but is obscured at times by the numerous granules. As is shown in the figures of the parotid the granules vary in number during the different stages of the cell's rest and activity. They accumulate during rest and disappear during activity. The same general observation may be made upon the secreting cells of all of the digestive glands. The serous cells take the protoplasm-stain, carmine, very deeply. The secretion from a serous gland is thin and watery. The cells of the *mucous*, submaxillary gland, on the other hand, are pyramidal in shape. A distinct lumen always exists in the alveolus. The nucleus is located near the outer end of the cell. The general appearance of the resting, mucous cell is much less opaque than that of the resting, serous cell. There are, however, numerous granules, but these are less abundant near the lumen of the alveolus and more abundant in the neighborhood of the nuclei. This is well shown in Piersol's figure (Fig. 170). Just what is the significance of the demi-lunes of Heidenhain is still a matter of controversy. They may represent exhausted cells pushed to one side by the active cells, or they may represent nascent cells which are destined to take the place of cells which lie nearer to the lumen.

The fact of greatest significance to the physiologist is the accumulation of granules in the gland-cells during rest and their disappearance during activity. That these granules bear some relation to the organic constituents of the secretion of the cells can be accepted as beyond question. Just what that relation is has not yet been definitely determined. The principal organic constituents of the saliva are mucin, ptyalin and albumin. The work of Langley (*Journal Physiology*, Vol. X., p. 433) upon the fresh gland shows that the granules of the mucus-secreting cell may be converted into mucin by simple addition of water. There can be no doubt that such a change takes place during secretion. The granules of the mucous cells may then be looked upon as the mother of mucin—mucinogen. The granules of the ptyalin-secreting cells probably represent the mother substance of ptyalin. But the changes which take place in the cell during secretion are not confined to the solution of the granules and the expulsion of the product into the lumen of the alveolus. Extensive anabolic processes take place.

The cytoplasm is replenished and the increase in size of the nucleus indicates that the nucleoplasm is replenished also. During the resting stage the protoplasm undergoes a change, probably katabolic, by which the granules are again formed and the cell becomes "loaded," ready for another period of secretion.

This cycle of cell activity is controlled by influences outside of the cell. It is important for the organism that all of the secreting cells of a gland act in harmony, and that the secretory phase of the activity occurs at the time when food is in process of mastication. The coördination of the activity of the gland with the associated functions can only be brought about by the agency of the nervous system.

The nerve supply of the salivary glands represents two general sources: (I) cerebral; (II) sympathetic.

The cerebral innervation of the salivary glands is represented on the parotid gland by branches received directly from the auriculo-temporal branch of the inferior maxillary division of the V. cranial nerve. But these fibers come ultimately from the *glosso-pharyngeal* or IX. cranial nerve and pass from that nerve to the auriculo-temporal through the tympanic nerve, the small superficial petrosal and the otic ganglion. The cerebral innervation of the submaxillary and sublingual glands is represented by branches received directly from the lingual branch of the inferior maxillary division of the V. cranial nerve. These fibers come ultimately from the facial or VII. cranial nerve and pass from that nerve to the lingual through the *Chorda tympani*, so called because it traverses the tympanic cavity. (See Tympanum under Hearing.)

The sympathetic innervation of the salivary glands is represented by branches from the superior cervical ganglion of the sympathetic system. These branches reach the glands by following the blood vessels.

In a general way one may say that the nerve supply of all the digestive glands is derived, like that of the salivary glands, from cranial and sympathetic sources. A study of Fig. 159, giving the innervation of the digestive system, shows that this is true of the innervation of the stomach, of the small intestine, of the liver and of the pancreas. Just how much influence upon these structures the vagus may exert through its connections in the solar plexus is at present quite unknown. The points which the innervation of the salivary glands possess in common with that of the other digestive glands, together with the fact that the nerves which supply the salivary glands are readily accessible to experimentation, has led physiologists to experiment extensively upon the influence of stimulation upon these glands, with a view to thus getting a clue to the influence of the nervous system upon secretion in general. The results are definite and conclusive with respect to the salivary glands themselves, and suggestive, if nothing more, with respect to digestive glands in general.

If the *Chorda tympani* be severed and its distal end electrically stimulated one may observe:

(I) A dilatation of the blood vessels, and (II) a profuse flow ot thin watery saliva from the glands which it supplies. If the sympathetic branches to these glands be severed and electrically stimulated one may observe: (I) a contraction of the blood vessels, and (II) a scanty secretion of thick viscid saliva. In the case of the parotid gland stimulation of the peripheral end of the divided parotid portion of the glosso-pharyngeal in any part of its course causes: (I) vaso-dilatation; and (II) profuse watery secretion, while stimulation of the peripheral end of the divided sympathetic branches to that gland causes: (I) vaso-constriction; but, in most animals, no secretion of saliva.

Various theories have been advanced to account for the phenomena observed and to harmonize the results of physiological experiments with the observations of the histological changes in the gland-cells during the cycle of cell activity.

That the increased pressure of the tissue-plasma resulting from the vaso-dilatation bears an important relation to the pouring out of a watery secretion by the cells has been generally accepted since the time of Ludwig's early experiments in this field in 1851.

The theory which presents itself at once is that the water and salts of the secretion are products of filtration from the tissue-plasma. If this be a tenable proposition, two things must be observed; first that the proportion of water and salts in the saliva must be the same as in the tissue-plasma; second, that the pressure of the secretion in the ducts of the gland will be less than the pressure of the blood in the vessels of the gland. But the water and the salts of the secretion are far different in proportion,—the water and salts of the plasma being about 90.3 per cent. and 0.85 per cent. respectively, while they occur in the secretion in the proportions of 99.4+ and 0.36.

As to the pressure, Ludwig (*Zeitsch. f. rat. Med., 1851—S. 271*) found in the same experiment a blood-pressure in the carotid artery of 112 mm. of mercury and a secretory pressure in the duct of the submaxillary rising to 190 mm. of mercury pressure when the gland is influenced by stimulation of the chorda tympani. Heidenhain (*Stud. d. physiol. Inst. zu Breslau*) found even greater differences between blood-pressure and secretory pressure. In the light of these observations it is evident that *the secretion of water and salts is not a process of filtration.* The next question which presents itself is: Do not the laws of diffusion and osmosis supplement and reinforce those of filtration?

The two most important factors in osmosis are: (I) The quantitative composition of the solutions separated by the membrane, and consequently the partial osmotic pressure exerted by the several constituents (*Reid, in Schaefer's Text-book of Physiology,* *Vol. I., p. 278*). (II) The coefficients of diffusion of the various constituents (Reid). The first one of these two factors operates in the following manner: If pure water be separated by a membrane from a solution of sodium chloride the water will diffuse much more rapidly toward the salt solution than will the salt solution toward the water, so that the liquid will rise on the side of the denser liquid. The process of interchange continues until the liquid on both sides of the membrane has the same quantitative composition. But during the progress of salivary secretion water passes constantly from the plasma where it forms only 90.3 per cent. of the liquid into the alveoli of the salivary glands where it forms 99.4 per cent. of the liquid.

It might be urged that the hydrostatic pressure overcomes any osmotic pressure that may exist on the opposite sides of the secreting cells. But we are seeking a factor to reinforce the hydrostatic pressure which was already too low to account for the secretory pressure. It is evident that the laws of osmosis will not assist us in accounting for the phenomena. To test the second factor of osmosis, the coefficients of diffusion of the various constituents, one may take for example a comparison of the two salts NaCl and KCl, both of which are constituents of both plasma and saliva. NaCl forms 0.55 per cent. and KCl 0.03 per cent. of plasma. The coefficient of diffusion of KCl is nearly $\frac{3}{2}$ that of NaCl. Maeignae (*Ann. de Chim., Paris, 1874, T. II., p. 546*), demonstrated that *the rapidity of diffusion of the more diffusible of a pair of salts diffusing simultaneously is found to be increased, that of the less diffusible diminished* (Reid). For example, NaCl has about $\frac{5}{3}$ times the diffusibility of Na_2SO_4 when diffusing separately; when diffusing simultaneously the NaCl is increased and the Na_2SO_4 diminished, the ratio being nearly 3:1.

If a similar relation holds for NaCl and KCl in salivary secretion we shall be prepared to find in the saliva that the KCl instead of being $\frac{1}{18}$ of the NaCl is increased to say $\frac{1}{12}$ or even $\frac{1}{10}$. But in the saliva the KCl : NaCl : : 3 : 5 (!).

When the two principal factors of osmosis are considered they are found to be completely inadequate to account for the phenomena of salivary secretion. The other factors of osmosis, character of membrane, pressure, temperature, are naturally the same for both salts and drop out of this calculation. We are forced to a further conclusion that: *the secretion of the water and the salts of the saliva is not a process of osmosis.* Finally: *the secretion* of the *water and the salts* of the saliva cannot be accounted for through the combined influence of the laws of *filtration* and the laws of *osmosis.* But these are the only known physical laws that may apply to this case. The cells which separate the plasma from the saliva are living cells. *Every living cell undergoes metabolic changes;* building up a portion of the material, taken from the medium in which the cell exists, into protoplasm and retaining a portion as cell-plasma or cell-sap. *Every living cell has the power to select,* from the medium in which the cell exists, *the materials which are to be used by the cell in its metabolism.* In a complex organism the cells comprising the different tissues are differentiated in function. A differentiation of function involves a differentiation of cell metabolism with all that that entails. In terms of these fundamental principles of biology one may say that the cells of the salivary glands receive from the organism nutriment and protection while they give to the organism the results of specialized activity. The selection of particular constituents in particular proportion and the throwing out of a particular mixture of katabolites (excretions) is nothing new; it is an attribute of every living cell. This is no attempt to tell just how the cell accomplishes this feat. The phenomenon is as inexplicable as life itself. This is an attempt to show that in the formation of a special secretion we have to deal with no new manifestation of cell life but with a slight specialization of inherent cell-attributes.

Of the various theories advanced to account for the phenomena of salivary secretion, that of Heidenhain as modified by Langley seems to be most reasonable. The essential features of this theory may be thus summarized:

(*a*) THE CEREBRAL NERVES *supply the glands with vaso-dilator fibers and with secretory fibers.* In harmony with this hypothesis is the fact that if atropine be injected into the gland stimulation of the chorda tympani will cause no secretion, though the vaso-dilatation leads to increased vascularity of the gland.

The secretory fibers have been paralyzed by the atropine.

(*b*) THE SYMPATHETIC NERVES *supply the glands with vaso-constrictor fibers and with secretory (trophic) fibers.*

(*c*) THE SECRETORY FIBERS, or at least secretory impulses, *may be classified as: (α) Those which control the secretion of water and salts; (β) those trophic fibers which control the metabolism of the cells:* (I) *anabolic secretory,* (II) *katabolic secretory.*

In the dog the cerebral nerve contains many fibers of class (*α*) and few of class (*β*), while the sympathetic contains many of class (*β*) and few or none of class (*α*).

To get a connected idea of the cycle of activity of the salivary gland let us begin with the period of rest or recuperation. (I) The reflex influence of the cerebral nerves is suspended because the sensory nerves of the mouth are no longer stimulated by the presence of food and the process of mastication. (II) With suspension of the activity of the vaso-dilator fibers the general and practically constant vaso-constrictor impulses through the sympathetic nerves reduces the blood supply to the gland. (III) The katabolic impulses cause the cells to change some of the protoplasm, both cytoplasm and nucleoplasm, to those granular forms which, during the secreting period, may be so readily changed to constituents of the secretion. (IV) Anabolic impulses are unquestionably received by the cell during the resting stage, but the very great production of granules and the noticeable depletion of both cytoplasm and nucleoplasm makes it likely that the katabolic processes preponderate.

Consider now the changes which are wrought during the secreting period: (I) The reflex influence of the cerebral nerves is brought into action through the stimulation of the sensory nerves of the mouth, and vaso-dilatation results. (II) Along with the increased blood supply come impulses through those secretory nerves (*a*) which control the secretion of water and of salts. The increased pressure of the tissue-plasma as well as the increased quantity of the tissue-plasma facilitates this phase of the secretory activity of the cells, and they "*select*" certain proportions of water and salts and pass them into the lumen of the alveolus. (III) Through the sympathetic system especially come katabolic impulses which lead to the final step of katabolism necessary to change the granular material to the stage represented in the secretion. For example, mucinogen granules are changed to mucin, and the ptyalin granules (ptyalinogen) to ptyalin. (IV) Through the sympathetic system especially come anabolic impulses which cause the cell to select nutrient materials from the abundant plasma and replenish cytoplasm and nucleoplasm, the former collecting in the form of clear, non-granular protoplasm at the base of the cell, while the latter fills out the somewhat shrunken nucleus.

This presentation, based upon the Heidenhain theory, must be understood as a purely tentative one. It seems to harmonize all of the phenomena as now understood.

The secretion of saliva has been discussed at some length, because it is better understood than is the secretion of the other digestive juices and may be accepted as probably typical in a general way of all of them.

b. The Composition of Saliva.

Herter (*Hoppe-Seyler, "Physiol. Chem.," Bd. II., S. 191*), gives the following analysis of human submaxillary saliva:

Human Submaxillary Saliva.	Water.				99.44 %
	Solids. 0.56 %	Organic.		Ptyalin. Mucus.	0.175
		Inorganic. .385 %	Soluble.	NaCl 0.155 KCl 0.094 Na_2CO_3 0.090 K_2SO_4 0.026	0.36
			Insoluble.	$CaCO_3$ 0.015 $Ca_3(PO_4)_2$ .010	1.025
					100.000

Hammerbacher (*Zeitsch. f. physiol. chem., Bd. V.*) gives the following analysis of human mixed saliva :

Human Mixed Saliva.	Water.			99.42 %
	Solids. 0.58 %	Organic.	Mucin and epithelium.	0.22
			Ptyalin and globulin.	0.14
			(Potassium Sulpho-cyanide .004 %.)	
		Inorganic.	NaCl, KCl $Na_2\,CO_3$, $CACO_3$ $Mg_3\,(PO_4)_2$, $Ca_3(PO_4)_2$	0.22
				100.00

2. THE CHEMISTRY OF SALIVARY DIGESTION.

The only chemically active agent in saliva is *ptyalin*. Ptyalin is an amylolytic enzyme, and its action is therefore confined to the change of starch to sugar and to the products intermediate between starch and sugar. Brown and Morris, quoted by Halliburton, sum up this change in the following reaction :

$$10(C_6H_{10}O_5)_n + 4nH_2O = 4nC_{12}H_{22}O_{11} + (C_6H_{10}O_5)_n + (C_6H_{10}O_5)_n$$

Starch + water = maltose + achroödextrin + erythrodextrin.

Most investigators agree that the first change is to soluble starch, "amidulin" or amylodextrine, which gives a blue color with iodin ; and that no erythrodextrin remains at the end of the reaction, but that there may be several forms of achroödextrin present.

Neumeister (*Lehrbuch d. physiol. Chemie*, 1893, S. 232) gave the following diagram as representing approximately what takes place in the action of ptyalin or amylopsin upon starch :[1]

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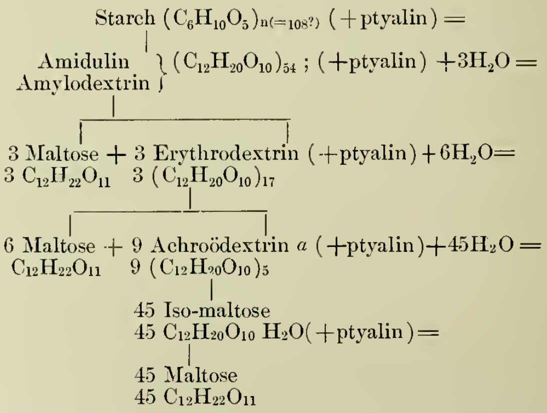
[1] In order that the reader may get a more concrete idea of the series of changes which this diagram contemplates it may be well to insert the quantitative molecular formulæ worked out by Lintner and Düll (*Ber. d. deutsch. chem. Gesell., Bd. 26, S.* 2533).



Starch $(C_6H_{10}O_5)_{n(=108?)}$ (+ptyalin) =

Amidulin / Amylodextrin $\}$ $(C_{12}H_{20}O_{10})_{54}$; (+ptyalin) $+3H_2O$ =

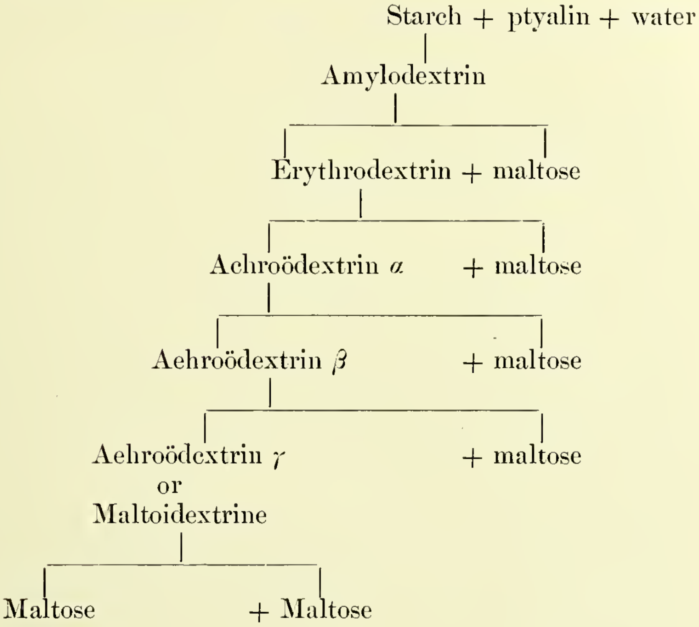
3 Maltose + 3 Erythrodextrin (+ptyalin) $+6H_2O$ =
$3\ C_{12}H_{22}O_{11}$ $3\ (C_{12}H_{20}O_{10})_{17}$

6 Maltose + 9 Achroödextrin *a* (+ptyalin) $+45H_2O$ =
$C_{12}H_{22}O_{11}$ $9\ (C_{12}H_{20}O_{10})_5$

45 Iso-maltose
$45\ C_{12}H_{20}O_{10}\ H_2O$ (+ptyalin) =

45 Maltose
$45\ C_{12}H_{22}O_{11}$

This series of reactions does not include the variations of achroödextrin for the very good reason that these dextrines are largely hypothetical.


Starch + ptyalin + water
Amylodextrin
Erythrodextrin + maltose
Achroödextrin α + maltose
Achroödextrin β + maltose
Achroödextrin γ or Maltoidextrine + maltose
Maltose + Maltose

The changes which glycogen $(C_6H_{10}O_5)_n$, undergoes during digestion are the same as those which starch undergoes. (Külz and Vogel, in *Zeitsch. f. Biologie*, 1895, Bd. 31, S. 108.)

It was originally supposed that starch was changed to dextrose, but it has been demonstrated that maltose is first formed and that only a very small proportion of dextrose is formed either through ptyalin or amylopsin. (Musculus and Gruber, *Zeitsch. f. physiol. Chem.*, Bd. II., S. 177.) It must be remembered that though ptyalin is capable of working all of the changes ascribed to it when the time is sufficient, the amylolytic changes are interrupted very early in their course by the acid reaction of the stomach and are not resumed until the products are again subjected to the influence of an amylolytic enzyme in the small intestine. Under the usual conditions the products of ptyalin digestion would include maltose, achroödextrin α, β and γ, erythrodextrin, and probably amylodextrin, there would also remain much unchanged starch. All of these excepting the starch are soluble, and maltose is crystalline and diffusible. It is either hydrated in the alimentary canal by invertin, or an allied enzyme, and changed to dextrose, in which form it is absorbed; or it is taken up by the absorptive epithelium as maltose and changes within the epithelium to dextrose, in which form it is passed into the capillaries of the portal system. It is certain that it does not enter the circulation as maltose.

3. FACTORS WHICH INFLUENCE SALIVARY DIGESTION.

a. The Preparation of the Food.

The importance of a most thorough cooking of starch and starchy foods can scarcely be too strongly emphasized.

The starch is deposited in stratified grains which have alternating layers of pure starch or granulose and of starch-cellulose, which also forms the outer layer of the starch grain. Starch-cellulose is quite indigestible by the ptyalin or amylopsin, and it is only with difficulty permeated by these enzymes, so that digestion of uncooked starch grains is very much retarded. Moist heat has the effect of swelling the granulose and bursting the starch-cellulose envelopes, thus liberating the pure starch which makes an opalescent paste if the water is sufficient in quantity. In any case it is made readily miscible with the saliva, and thus the action of the ptyalin is much facilitated.

b. The Mastication of the Food.

If the starchy food be bolted in unbroken pieces it is evident that, however thoroughly the food may be cooked, and however active and abundant the enzyme may be, the amylolytic action of the ptyalin must be slight, because not brought into proper physical relation to the starch.

A thorough mastication of the food breaks it up into minute pieces and mixes the saliva with it, so that the enzyme is brought into contact with a much larger proportion of starch than could be possible otherwise.

The time required for thorough mastication is another important element because the change in the starch may be well advanced before the food leaves the mouth.

c. The Temperature of the Mixture.

After the well cooked food is thoroughly masticated there are other important conditions which must be fulfilled if the digestive changes are to be rapid and extensive. The *temperature* affects the operation of any enzyme. The *optimum temperature* is approximately that of the blood (37° C.–40° C.). Outside of these limits the action is progressively slower the farther removed from the optimum. The action is wholly suspended at 0° C. but the enzyme is not destroyed. The action is wholly suspended at 65°–70° C. and the enzyme is destroyed. Much has been said about the effect of cold drinks upon digestion. A large portion of what has been said cannot be verified by experiment. Experiment has demonstrated that if the contents of a beaker be diluted with 10 volumes of water at 0° C. the action of the ptyalin will be much retarded, partly because of the dilution and partly because of the marked change of temperature. When cold water is taken with meals it is usually taken in moderate quantities so that the dilution is not sufficient to retard the action of the enzyme. It is usually taken sufficiently slowly to be warmed to almost blood temperature before it reaches the stomach so that a glass of cold water taken a little at a time during the progress of a meal cannot be said to effect any demonstrable retardation upon salivary digestion in the stomach.

d. The Reaction of the Mixture.

The saliva is faintly alkaline because of the Na_2CO_3 which it contains. It is not necessary, however, that the reaction of the mixture of food and saliva be alkaline. The ptyalin acts quite as well in a neutral as in a faintly alkaline medium. Even a weak acid reaction does not stop—though it retards—the action of the enzyme, provided the acid be an organic acid like lactic acid. When HCl is combined with a proteid, as acid-albumin or syntonin, it will cause an acid reaction, but when the reaction is only faintly acid the action of the ptyalin may proceed, though at a slower rate. *Free HCl* will, however, stop the action of the ptyalin and destroy it when it is present in even so small a proportion as 0.003 per cent. (Chittenden, in *Studies from the Lab. of Physiol. Chem. Yale*, Vol. I., 1884). The free use of sour pickles and acid drinks must retard the action of the ptyalin. In the light of what will follow (*e*) it is evident that these acid foods may be taken late in a meal with less effect upon salivary digestion than when taken early in a meal.

e. The Time of Salivary Digestion.

The food is retained in the mouth not more than one minute at the longest. In this time the change has only begun, even when all the conditions are most favorable. The hydrochloric acid of the gastric juice is not present in the stomach until the stimulating presence of food induces its secretion. After it begins to be secreted some minutes elapse before the quantity of combined acid is sufficient to essentially retard the salivary digestion. It is estimated that from 30 minutes to 45 minutes, or even more, may elapse before salivary digestion is wholly suspended by the accumulation of *free* HCl.

The following conditions favor a prolongation of the time of salivary digestion: (I) The retardation of the secretion of hydrochloric acid. Nothing so quickly brings about a secretion of this acid as a glass of cold water. It is evident then that the drinking of water at the beginning of a meal will tend to shorten the period of salivary digestion. (II) The retardation of the permeation of the food by the acid. If the food is semi-solid the acid permeates it slowly; if it is fluid the acid becomes readily mixed by diffusion as well as by movements of the stomach.

Soups and drinks bring the contents of the stomach into a soupy mass which is readily acidified as soon as the HCl begins to be secreted. In this case again fluids at the beginning of the meal are unfavorable to the prolongation of the time of salivary digestion.

It is doubtful if in the average case there is any advantage in thus prolonging salivary digestion. The amylopsin of the pancreatic juice is a more active amylolytic enzyme than is ptyalin, and it has all the time necessary for its action without encroaching upon the time of other digestive processes.

4. MASTICATION.[1]

This process is a purely mechanical and physical one which is wholly a voluntary one. With this process are associated those gustatory sensations and perceptions which are so enjoyable to most of mankind. The movements of the jaws, cheeks and tongue stimulate the flow of saliva and insure the thorough mixing of that secretion with the food (*insalivation*). The insalivation of the food produces three effects: (I) To *digest with ptyalin* the starch of the food; (II) to *lubricate* with *mucus* the mass of food, thus preparing it for deglutition; (III) to *dissolve* with the *water* of the saliva the soluble portions of the food,—salt, sugar, etc.

In the discussion of the factors which influence salivary digestion the importance of the division of the food into fine particles was mentioned. It is quite as important in digestion by the other digestive fluids that the food be triturated. The enzyme gets access only to the surface of the particles of food if the same volume of food present twice the surface one would expect it to digest in one-half the time, and such is approximately the case. Eight 1 mm. cubes of coagulated egg albumin would contain the same amount of albumin as one 2 mm. cube. They would aggregate twice the surface, and the time of digestion would be approximately half as long in the case of the 1 mm. cubes as in the case of the 2 mm. cubes.

The structures involved in mastication may be classified as skeletal, muscular and nervous.

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[1] It is proposed to discuss the movements of the different segments of the alimentary canal in connection with the digestive changes effected in the several portions, progressing step by step from the oral to the anal end of the tract. The movements of the mouth are an important factor in salivary digestion. The movements of the stomach influence gastric digestion profoundly, and the movements of the intestine influence not only digestion, but also absorption in that segment of the canal.

a. The Skeletal Structures of Mastication.

These include the maxillary bones as representatives of the endoskeleton, and the teeth as representatives of the exoskeleton. The development of the teeth, in the race and the individual, has been treated above. The function of mastication is variously specialized in different orders of mammals. It reaches its highest development in herbivora—whose food is difficult to masticate and yet requires the finest trituration in order to be digestible. The teeth of herbivora are the most perfect dental organs in the animal kingdom. The incisors are cupped and the molars have alternating ridges of dentine and enamel, and are self sharpening. The carnivorous animals bolt their food with little chewing. The teeth which are well developed are the great, prehensile canines and the trenchant molars which are especially adapted for breaking the bones of the prey. The omnivorous animals, to which kind man belongs, possess edged *incisors;* meager *canines*, scarcely prehensile in man, though distinctly so in the gorilla; and *molars* with rounded cusps well adapted to crush, but not at all capable of cutting the food. The movements of the jaws differ distinctly in the different orders of animals above. The chopping movement is peculiar to the carnivora; the herbivora give the mandible a wide lateral, and antero-posterior excursion, while the omnivora possess all of these movements in a moderate degree.

b. The Muscles and Nerves of Mastication

include:

(*a*) The *flexors* or levators of the mandible: (I) The masseter; (II) the temporal, and (III) the internal pterygoids. All of these are innervated through the inferior maxillary division of the fifth cranial nerve.

(*b*) The *extensors* or depressors of the mandible: (I) The digastric; (II) the mylo-hyoid, and (III) the genio-hyoid. (I) and (II) innervated by the inf. max. division of the V, and (III) innervated by the hypoglossal.

(*c*) The *lateral movements* of the jaws are produced by the *alternate action* of the external pterygoids.—Inf. max. div. of V.

(*d*) *Protruders of the mandible:* The external pterygoids *acting together.*

(*e*) *Retractor of the mandible:* The posterior portion of the temporal.

(*f*) *The cheek and lip muscles:* Buccinator and orbicularis oris, innervated by the buccal branch of the facialis.

(*g*) *The lingual muscles* innervated by the lingual branch of the inferior maxillary division of the trigeminus and by the hypoglossus.

c. The Process of Mastication.

The food is cut by the incisors and crushed between the molars. The cheeks and tongue assist in bringing the food between the molars. The movements of the masticatory apparatus in itself tends to stimulate the flow of saliva; the presence of food, especially acid, sweet or dry food, tends also to stimulate the secretion of saliva.

The movements of mastication mix the saliva thoroughly with the food. The gustatory apparatus is stimulated by all substances which are soluble in water, and the olfactory apparatus by all volatile substances. The sensations derived from these two sense organs make up the so-called "tastes" and "flavors" of the foods. The pleasure derived from eating consists: (I) in the satisfying of the hunger, (II) in the enjoyment of the tastes and flavors. Hunger seems to be nature's warning of need for nutriment; while the pleasures of the taste and smell, besides assisting the animal in the choice of food, repay the animal for a thorough mastication of it.

5. DEGLUTITION.

After the food is made ready for the stomach, by mastication, it is gathered, by the tongue, into a bolus or rounded mass between the tongue and the hard palate, and passed back to the pharynx, whose walls by a convulsive reflex act pass it to the œsophagus, along which it is pressed, by a peristaltic wave, into the stomach. The whole process of *swallowing* as here briefly outlined is called *deglutition.* The length of time required to perform the act is not commensurate with its complexity. The process may be analyzed as consisting of a voluntary and an involuntary part.

a. The Voluntary part of Deglutition.

This consists in (I) *the formation of the bolus* by the cheeks, palate and tongue; and (II) in the *pressing of the bolus backward* through the isthmus of the fauces, *i. e.,* between the anterior pillars of the fauces which are the ridges marking the location of the palato-glossal muscles. Once the bolus of solid food (or the "swallow" of liquid) passes this *Rubicon* there is no turning back, the muscles of the pharynx grasp it reflexly and hurry it forward by wholly involuntary processes. The muscles and nerves of this voluntary initiatory step of deglutition have been enumerated under mastication in which function they are important factors.

b. The Involuntary Part of Deglutition.

This consists in the transit of the bolus through the pharynx; and in its passage along the œsophageal canal.

1. **Pharyngeal Deglutition.**—The transit of the food through the pharynx is attended with two dangers, namely, the danger of a falling of a portion into the larynx, and the danger of regurgitation of a portion into the posterior nares. Pharyngeal deglutition consists, then, of three acts: transportation of the food; guarding against a false passage into the larynx; guarding against a false passage into the posterior nares.

(*a*) TRANSPORTATION of the food through the pharynx and into the œsophagus is, according to Kronecker and Metzger (*Arch. f. Physiologie*, 1883, S. 328), accomplished in two phases, a *projection phase* and a *clearing-up phase.* When the bolus reaches the isthmus of the fauces the tongue is closely approximated to the palate, blocking the way to the front. A convulsive contraction of the mylo-hyoid muscles puts the bolus under pressure and *projects* it across the pharyngeal cavity; the way is cleared by the simultaneous contraction of the hyoglossi muscles which move the root of the tongue backward and downward. This movement depresses the epiglottis over the opening of the larynx, thus guarding that passage. In the case of liquid or semi-solid food the entire transit of both pharynx and œsophagus is made in 0.1 second. The force of gravitation assists in this preliminary act—*the projection of the bolus. The clearing-up phase* of pharyngeal deglutition consists in a general peristaltic constriction passing from above downwards and beginning 0.3 second after the constriction of the mylo-hyoids.

The first step in this phase consists of a contraction of the longitudinal muscles of the pharynx which serves to pull the walls of the pharynx toward the bolus of food. The second step follows the guarding of the respiratory openings.

(*b*) THE GUARDING OF THE POSTERIOR NARES is insured by the elevation of the soft palate through the contraction of the levator palati and tensor palati muscles; by the contraction of the palato-pharyngei muscles, and by the elevation of the uvula through the azygos uvulæ muscle.

(*c*) THE GUARDING OF THE LARYNGEAL OPENING is insured in part by the depression of the root of the tongue through the hyoglossi muscles as described above. Supplementing this and following it in time is the closure of the laryngeal opening by the adduction of the vocal cords. (For muscles and nerves see larynx.)

The second step in the clearing-up phase of food transportation through the pharynx consists of a peristaltic action of the constrictors of the pharynx. By this last act of pharyngeal deglutition any particles of food and any accumulated mucus are cleared from the pharynx and started along the œsophagus.

The two phases of deglutition above described (projective and clearing-up), seem to play parts of different relative importance according to the physical condition of different foods. In the case of liquid or very soft food the projection phase is the more important.

In drinking the cycle of swallowing acts follow in such rapid succession that there is not time for one to be completed before another is induced. Through the influence of the central nervous system all that portion of one deglutition, incompleted when a second deglutition supervenes, is suspended or inhibited.

Kronecker and Meltzer found that about 1.2 seconds elapse between the beginning of the contraction of the mylo-hyoid and the beginning of the contraction of the upper segment of the œsophagus. There would be five complete pharyngeal acts in six seconds; this is just about the usual rate of deglutition when drinking. The œsophageal peristaltie waves must then be suspended during the progress of drinking. The observers cited found, furthermore, that the constrictors of the pharynx, though they would have time to contract, actually remain at rest; the deglutition being in this case a series of projections followed at the end by a clearing-up contraction of pharynx and œsophagus.

In the case of solid food in a well-formed bolus of considerable consistency the clearing-up phase always follows the projection of the bolus across the pharyngeal cavity.

2. **Œsophageal Deglutition.**—The bolus is passed along the œsophagus by a peristalsis which differs from peristalsis of the lower segments of the alimentary canal in being more under the immediate control of the central nervous system, as evidenced by the fact that removal of a segment of the œsophagus does not block the progress of the peristalsis, while the severing of a nerve suspends the peristalsis in the segment supplied by the severed nerve.

c. The Influence of the Nervous System upon Deglutition.

(*a*) THE CENTER for involuntary pharyngeal and œsophageal deglutition lies in the upper end of the medulla, anterior to the respiratory center. The boundaries of the center have not been clearly defined.

(*b*) THE AFFERENT OR SENSORY IMPULSES which precipitate the act of involuntary deglutition reach the center through the pharyngeal and the superior laryngeal branches of the *vagus*, and the palatal branches of the superior maxillary divisions of the *trigeminus*. The contact of the bolus of food with the mucous membrane supplied by the above-named nerves is a sufficient stimulus normally.

(*c*) THE EFFERENT OR MOTOR IMPULSES which put the muscles of deglutition into activity are the *hypoglossal* to the tongue and to the muscles which raise the larynx, the *glosso-pharyngeal, vagus, facial* and *trigeminus* to the *palate, fauces* and pharynx, and the *vagus* to the larynx and œsophagus.

B. GASTRIC DIGESTION.

1. THE GASTRIC JUICE.

a. The Secretion of Gastric Juice.

1. **The Structure of the Gastric Glands.**—The general features of the secretion of gastric juice are the same as those of the secretion of saliva. The differences are specific rather than generic and are incident to the location and the specialized function.

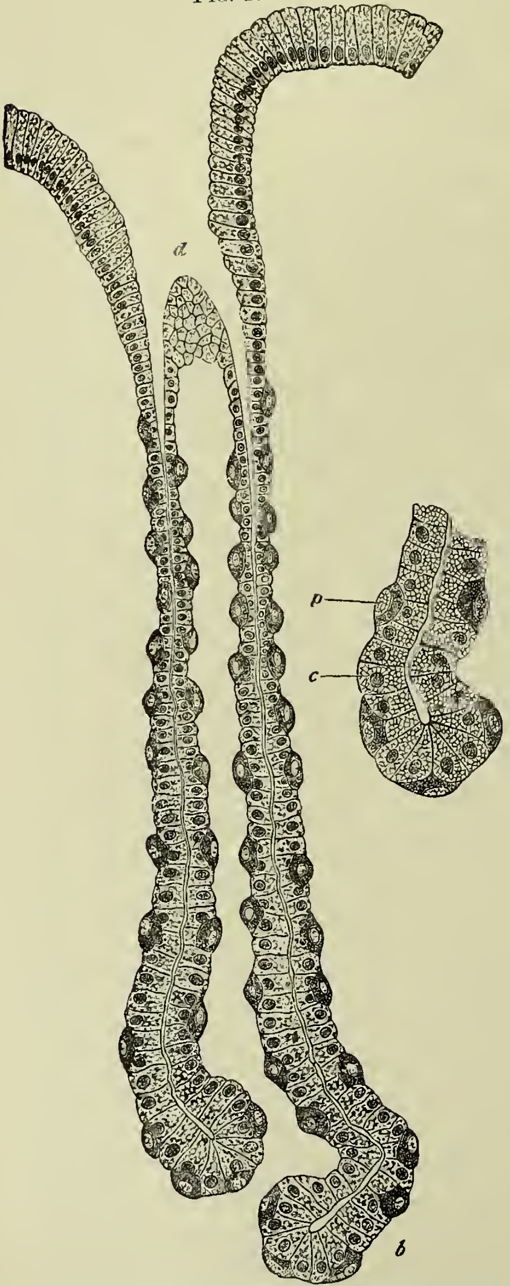
The gastric glands are usually classified as cardiac and pyloric, because the glands of these two regions differ both functionally and structurally. The cardiac glands (see Fig. 171) possess two kinds of active cells, the "*chief*" or *central cells* and the *parietal cells.*

The columnar central cells are filled with a fine reticulum, and possess an amount of granular matter varying with the phase of activity. The discoidal or crescentic parietal cells do not lie beside the main lumen of the gland, but each cell possesses a diverticulum from the main lumen. (See Fig. 172.)

Besides the diverticula shown in Fig. 172 there are minute capillary branches of each diverticulum, which surround the parietal cells. (See Fig. 173.)

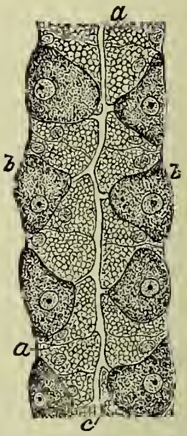
There has been some controversy about the function of these cells. The following facts deserve consideration in this connection: (I) The cells vary in size during different phases of glandular activity, being larger at the beginning than at the end of secretion. (II) Each cell is provided with a special system of little ducts or lumena. (III) The parietal cells are the only cells peculiar to the cardiac end of the stomach. (IV) The secretion from the cardiac end of the stomach contains hydrochloric acid, while the secretion from the pyloric end of the stomach contains no hydrochloric acid. This was demonstrated by Heidenhain, who separated the two portions of the stomach, giving each in turn an external fistulous opening. From the cardiac end of the stomach only was the secretion acid in reaction. These facts seem to justify the following inferences: (I) The parietal cells are directly associated in the function of secretion of gastric juice. (II) They secrete a liquid that must find its way into the main lumen of the gland. (III) They secrete a liquid peculiar to the secretion of the cardiac end of the stomach.

FIG. 171.



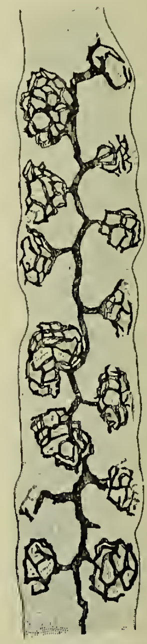
A cardiac gland from the dog's stomach. (Highly magnified.) (KLEIN.) *d*, duct or mouth of the gland; *b*, base or fundus of one of its tubules. On the right the base of a tubule more highly magnified; *c*, central cell; *p*, parietal cell.

FIG. 172.



Portion of cardiac gland of dog, highly magnified: *a*, *a*, the central or chief cells next the lumen (*c*); *b*, *b*, the parietal or acid cells connected with the lumen of the tube by short lateral branches which extend to the cells. (PIERSOL.)

FIG. 173.



A cardiac gland prepared by Golgi's method, showing mode of communication of the parietal cells with the gland-lumen. (SCHAEFER after E. MÜLLER.)

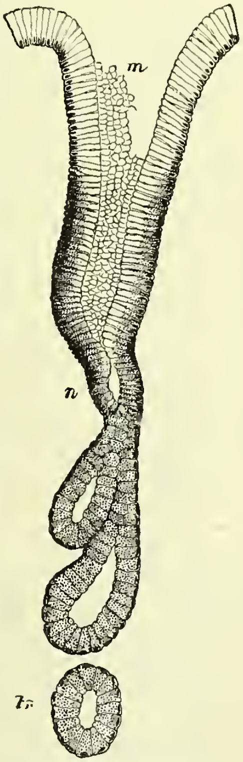
(IV) Hydrochloric acid being the only liquid peculiar to the cardiac end of the stomach, *the parietal cells must, therefore, secrete hydrochloric acid.* This course of reasoning is sufficiently convincing to satisfy most physiologists of the probability that in the parietal cells we see the site of the formation of hydrochloric, but it is reasoning by exclusion and cannot be accepted as an absolute demonstration.

The central cells are common to the cardiac and the pyloric glands. The secretion of pepsin is a function common to the cardiac and pyloric ends of the stomach. The central cells of these glands are larger at the beginning than at the end of secretion. They contain many granules at the beginning of secretion and few at the end of that process. There can be little doubt that the pepsin of the gastric juice is formed in the central or chief cells of the cardiac and pyloric glands.

The pyloric glands differ from the cardiac glands, first in general form—the ducts of pyloric glands being long and relatively wide. Into this duct empty several more or less tortuous tubules (See Fig. 174).

2. **The Secretion of Pepsin.**—This is one of the essential constituents of the gastric juice and its formation within the cells corresponds closely to the formation of the ptyalin in the cells of the salivary glands. The granules formed in the cells during the period of rest represent a mother-substance of pepsin or a zymogen which has been called *pepsinogen.* During the secretion of gastric juice the zymogen is subjected to a further metabolism which changes it to pepsin; at any rate pepsin is one product of this final metabolism. The pepsin-secreting power of the pyloric glands is much below that of the cardiac glands. It is contended by some[1] that any pepsin found in the pyloric segment of the stomach, or extracted from the mucous membrane of that segment was secreted by the cardiac glands and simply absorbed by the pyloric mucous membrane, or taken up by "*infiltration.*" Heidenhain's investigations have, however, demonstrated conclusively that *pepsin is secreted by the pyloric glands.*

FIG. 174.



A pyloric gland, from a section of the dog's stomach. (EBSTEIN.) *m*, mouth; *n*, neck; *tr*, a deep portion of a tubule cut transversely. (SCHAEFER.)

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[1] Wassmann. "*De digestione monnula*" Berolini, 1839; Von Wittich, "*Uber die* Pepsin wirkung der Pylorus drüsen," *Arch. f. d. ges. Physiologie*, Bonn, 1873.

3. **The Secretion of Rennin.**—Much that has been said regarding the secretion of pepsin is equally true for the milk-curdling enzyme, *rennin*. Rennin is secreted by the central or chief cells of the cardiac and pyloric glands. It is secreted more abundantly by the cardiac than by the pyloric glands. It exists in the gland cells in a granular zymogen (renninogen) which may be extracted as such and then changed to the active form, rennin. In fact, the first zymogen found was that of rennin.[1] The granules of pepsinogen and renninogen exist together in the gland cells and it is impossible to differentiate them morphologically. They may, however, be separated chemically.

4. **The Secretion of Hydrochloric Acid.** — Hydrochloric acid is almost without doubt secreted by the parietal cells of the cardiac glands. From what materials and by what process the acid is formed is an undecided question.

"There is little doubt that the material for the formation of the HCl is the sodium chloride, which forms a large part of the ash or blood and lymph. The plasma and lymph is alkaline through presence of sodium carbonate. How can chlorine be liberated from the sodium chloride of the alkaline plasma? Only two methods are possible: 1st, either the Cl must be separated from Na through some active energy as electricity,—in electrolysis,—or, 2d, the Cl must be displaced by another acid. There is no ground for believing that the separation is effected by electricity" (Bunge: Physiological Chemistry). But it is generally believed that only a stronger acid can displace a weaker one. In 1871 Julius Thomsen demonstrated that "every acid can displace, from its combination with any base, a part of any other acid." (J. Thomsen, "Thermo-chemische Untersuchungen," *Poggendorff Ann.*, 143, 1871.) This ability is not through affinity alone but through another characteristic which Thomsen called "*avidity*." When equal parts of HCl and acetic acid act together upon Na_2CO_3 in aqueous solution only $\frac{1}{34}$ of the Na will combine with the acetic acid; so the latter acid has only $\frac{1}{34}$ the *avidity* of HCl. But if the proportion of acetic acid be increased, more than $\frac{1}{34}$ of the Na will combine as sodium acetate; and the more, the greater the preponderance of acetic acid.[2]

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[1] Hammersten, Jahresber. üb. d. Fortschr. d. Thier.-Chem., Wiesbaden, 1872.

[2] As an example of the above let us take equal parts of these acids and Na_2CO_3 in excess. The following equation would represent the relations in question:

$$\left.\begin{array}{l}70\ HCl\\ 70\ H{\cdot}C_2H_3O_2\end{array}\right\} + 35\ Na_2CO_3 = \left\{\begin{array}{l}68\ NaCl\\ 2\ Na{\cdot}C_2H_3O_2\end{array}\right\} + 2\ HCl + 68\ H{\cdot}C_2H_3O_2$$
$$+ 35\ H_2O + 35\ CO_2.$$

Now if the avidity of $C_2H_3O_3{\cdot}H$ is only $\frac{1}{34}$ that of HCl then let us take 34 times as many molecules of the former as of the latter: The following equation would represent the relations in question:

$$\left.\begin{array}{l}HCl\\ 34\ C_2H_3O_2{\cdot}H\end{array}\right\} Na_2CO_3 = \left\{\begin{array}{l}NaCl\\ Na{\cdot}C_2H_3O_2\end{array}\right\} + \left.\begin{array}{l}\cdots\cdots\cdots\\ 33\ C_2H_3O_2{\cdot}H\end{array}\right\} + H_2O + CO_2$$

This displacement of a stronger acid by a weaker one when the latter is increased in proportion is called the "mass-effect" of weak acids. "Even CO_2 (or H_2CO_3) one of the weakest acids, must be able through *mass effect* to displace a small part of any other acid" (Bunge). The reaction might be written thus:

$$2\,NaCl + 1000\,H_2CO_3 = 999H_2CO_3 + 2HCl + Na_2CO_3.$$

Maly, — followed by Halliburton,—has suggested that the $CaCl_2$ and Na_2HPO_4 of the blood are brought together in the secreting cells and form the following reaction:

$$2\,Na_2HPO_4 + 3\,CaCl_2 = Ca_3(PO_4)_2 + 4\,NaCl + 2\,HCl.$$

Maly also suggested the following reaction as an alternative:

$$NaH_2PO_4 + NaCl = Na_2HPO_4 + HCl.$$

That any one of these reactions occurs has not been demonstrated. Most physiologists believe that the chlorine is liberated chemically in some way from one of the chlorides of the blood. But, as Bunge says, "There is less obscurity in the liberation of free HCl than in the ability of the parietal cells to secrete the HCl toward the lumen of the gland and discharge the other products toward the blood." In other words, even after we have accounted chemically for the formation of the hydrochloric acid we will still have to fall back upon the vital activity of the cell to account for its ability to select from the blood the compounds needed in the reaction, and to return to the blood a part of the products of the reaction while another part is secreted into the lumen of the gland.

5. **The Influence of the Nervous System Upon the Secretion of the Gastric Juice.**—Recall the innervation of the stomach: (I) The left vagus distributed to the smaller curvature superficially; the right vagus passing behind the viscus and incorporated in the solar plexus, in part to return, accompanied by sympathetic fibers from the splanchnics, and distributed to the greater curvature superficially. (II) The gangliated *plexus* of *Auerbach* lying between the muscular coats of the stomach. (III) The gangliated *plexus* of *Meissner* lying in the submucosa. (IV) The special plexuses of Openchowski,[1] which innervate the *cardia* and *pylorus*.

Note that the innervation is *cerebral* and *sympathetic;* thus far it is like the innervation of the salivary glands. Note, further, that there are present in the stomach at least two distinct diffuse,

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[1] "Ueber die nervösen Vorrichtungen des Magens," *Centralbl. f. Physiol.*, 1889, B. III.

gangliated plexuses. Ganglia represent either relay stations or reflex centers, or both. Organs which are richly supplied with ganglia are usually somewhat independent of the central nervous system, and respond readily to local influences.

To Pawlow[2] we are indebted for a solution of the problem concerning the function of the various nerves which supply the stomach. Pawlow divided the œsophagus in the dogs on which he operated, making a double fistulous opening on the neck. This enabled him to feed the dogs by mouth, but diverted the swallowed food so that it did not reach the stomach. This he called "*pseudo-feeding*." Through the distal end of the œsophagus he was able to introduce into the stomach food which had not been in the mouth—"*true feeding*." A third variation consisted in presenting to the longing eyes and nose of the animal food which he was allowed to receive into neither mouth nor stomach—"*psychic feeding*."

The following results were obtained: (I) After feeding, whether psychic, pseudo, or true feeding, gastric juice is freely secreted.

But in the case of psychic feeding, after the dog learned by experience that the food presented was not actually to be given him the secretion did not take place. (II) *A latent period* elapses between the beginning of stimulation and the beginning of secretion. (III) The latent periods for the three different methods do not differ essentially (about 7 min. in the dog).

These facts point directly to the central nervous system as the strongest factor in inducing and controlling the secretion of gastric juice.

Pawlow varied his experiments by severing in turn the sympathetic and the vagus innervation: (IV) Cutting off the influence of the sympathetic system through the splanchnic did not stop the secretion of gastric juice when the proper stimulus was applied in one of the forms of feeding. (V) Cutting off the direct influence of the brain through the vagi stopped all reflex secretion of gastric juice, though the severing of one vagus did not suffice to produce this effect. (VII) Stimulation of the distal ends of the divided vagi caused secretion of gastric juice.

The inferences to be drawn from these observations are obvious.

That the mechanical stimulation of the mucous membrane by the contact of the solid food causes little secretion is demonstrated by Pawlow's experiment, in which pebbles were introduced into the stomach followed by no measureable secretion. After a series of experiments Heidenhain (*Arch. f. d. ges. Physiol.*, 1879, Bd. XIX.) concluded that "*certain products of digestion* when *absorbed stimulate the flow of gastric juice*?" Chischin (Inaug. Dissertation,

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[2] "Die Innervation der Magendrüsen beim Hunde," *Archiv für Physiol.*, Leipzig, 1895.

St. Petersburg, 1894. Quoted from Edkins, in Schaefer's Textbook of Physiology) after experimenting with various foods and products of digestion sums up the question thus: "*At the time of taking food the first flow of gastric juice is determined by the reflex psychic influences involved in taking food. The digested proteids —(peptones)—are able later to evoke a secretion at a time presumably when the psychic influence begins to wane.*" (Edkins.) This suggested the introduction of peptone *per os.* The experiment resulted in an immediate secretion of large quantities of gastric juice with *high acidity* and well marked digestive powers. The therapeutic significance of this observation is apparent.

Different foods influence in a different manner the secretion of the gastric juice. When bread alone is taken the gastric juice possesses a "low acidity but a high degree of peptic power; whereas with milk a high degree of acidity is shown but a much lower degree of digestive (peptonizing) power." (Edkins.) Attempts to systematize effects of a mixed menu have been unsuccessful.

b. Chemical Composition of the Gastric Juice.

The most reliable complete analyses of gastric juice are those made by Carl Schmidt.[1] The human gastric juice was collected from a *healthy woman* who had a permanent gastric fistula made necessary by a traumatic stricture of the œsophagus. The analysis of gastric juice from the carnivorous animal is the mean of ten determinations from a dog whose salivary ducts had been ligated.

CONSTITUENTS OF THE GASTRIC JUICE.	HUMAN.	DOG.
Water.	99.440	97.306
Solids.	0.560	2.694
Organic.	0.319	1.713
Pepsin, *Rennin*, Mucin, etc.		
Inorganic.	0.241	0.981
HCl	....[2]	0.334
NaCl	0.146	0.250
KCl	0.055	0.112
$CaCl_2$	0.006	0.026
NH_4Cl	......	0.047
$Ca_3(PO_4)_2$	0.013	0.171
$Mg_3(PO_4)_2$		0.023
FePO		0.008

Note that the principal organic substances are the enzymes. Mucin is always a constituent of the secretion of a mucous membrane. Among the salts one notes the presence of chlorides and phosphates but the absence of carbonates which formed an important constituent of the saliva causing its alkalinity. The acidity of the gastric juice is not always due to HCl, but frequently to lactic acid, which is the product of a lactic acid fermentation which takes place in the contents of the stomach. Note that the gastric juice of the dog is much richer in both organic and inorganic constituents than is human gastric juice. The HCl in the gastric juice of the dog ranges from 0.3 per cent. to 0.5 per cent. That it should be stronger is to be expected first because the diet of the carnivorous animal is largely a proteid diet which must follow either an *acid pepsin* digestion or a *trypsin* digestion. The bones which carnivorous animals eat can only be digested by a strongly acid gastric juice.

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[1] Quoted from Maly in Hermann's Handbuch, Bd. V., § 2, 570.

[2] For some unaccountable reason the analysis of Schmidt gives HCl as 0.02 per cent. which is about one-fifteenth the quantity which Bunge (Physiol. chemie) reports as the result of repeated tests of the HCl content of gastric juice. We may, therefore, accept the quantity of HCl as being about 0.3 per cent.

2. THE CHEMISTRY OF GASTRIC DIGESTION.

Experiment shows that the active agents of the gastric juice are the enzymes and the acid.

If a typical proteid, such as coagulated egg-albumin, be put into a *neutral* solution of pepsin it will not be dissolved.

If a proteid be put into a 0.1–0.3 per cent. HCl solution it will be modified both physically and chemically—it will swell up and become clearer, some proteids actually passing into a clear solution. The chemical change, though not understood in detail, is recognized as a chemical association, or possibly a typical chemical combination of the HCl molecule with the proteid molecule. Such a compound is called an *albuminate* and is classified as one of the *derived proteids*. This particular albuminate is called *acid-albumin*, or *syntonin*. Acid-albumin, or syntonin, is precipitated by neutralizing the solution. It can be re-dissolved by weak acid or be converted into *alkali-albumin* by weak alkali.

It must be evident from the above that of the active agents the acid must act first upon the albumin and globulin classes of proteids. If one bring gastric juice—either secreted or artificial—into contact with a native proteid under favorable conditions the proteids will be rapidly changed to syntonin. Upon this syntonin the pepsin acts, inducing a series of hydrolytic cleavages.

As in the hydrolytic cleavages which starch undergoes under the influence of ptyalin, so here the process represents several steps. Just how many steps there are between the acid-albumin or syntonin and the final product, peptone, is still an open question. The mid-products between the albuminates and the peptones are called *proteoses* in general.[1]

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[1] The mid-products of the native albumins are called the *albumoses;* of the globulins, *globuloses;* of casein, *caseinoses*, etc., etc., but these distinctions, if justified by our present chemical knowledge, are certainly not necessary at present. Let us, therefore, group all of the mid-products between the syntonins and the peptones as *proteoses*.

Of the proteoses two steps have been demonstrated, viz., primary proteoses and secondary proteoses. The secondary proteoses are appropriately so-called because they not only follow the primary proteoses in time, but are derived from them. The primary proteoses exist in two chemically separable forms named by Neumeister (Lehrbuch d. physiol. chemie) *proto-albumoses* (proto-proteoses) and *hetero-albumoses* (hetero-proteoses).

The deutero-albumoses exist in forms which are not chemically separable, but which give rise to a series of peptones also inseparable chemically. A part of the peptone formed by peptic proteolysis undergoes under the influence of trypsin, further change which results in the formation of tyrosin, leucin and allied nitrogenous bodies. The other part of the peptone is not acted upon by trypsin. The discovery led to Kühne's (Verhandb. die Naturh. Med. Ver. zu Heidelberg, 1877, Bd. I., S. 233) hypothesis, published over twenty years ago, that there is during peptic proteolysis a cleavage of the molecule into two *coördinate* ones which he designated *hemi-* and *anti-*peptone, etc. Certain chemical considerations led Kühne and his school to believe that this *coördinate cleavage* takes place very early in the proteolysis and that once the cleavage occurs there are two practically parallel series of changes, one resulting in anti-albumoses and anti-peptone, the other resulting in hemi-albumoses, hemi-peptone. Two decades of investigation by Kühne and his pupils have resulted in most notable contributions to the subject of peptic and tryptic proteolysis, and the chemistry of the products of proteolysis.

The hypothesis of Kühne, though it has formed the working basis of this school during the period mentioned, falls far short of an adequate demonstration. In summing up the *experimental* evidence on this subject Moore says in his chapter on "The Chemistry of the Digestive Processes" (Schäfer's text-book of Physiol., Vol. I., p. 420): "This [the series of proteolytic changes] is all easily accounted for on the supposition that a variable fraction of the proteid molecule is easily attacked and broken off into amido-acids [leucin, etc.] by trypsin, but it is very difficult to explain on the supposition that the proteid molecule, early in the process of decomposition breaks up into two halves, of which one changes through the stages of hemialbumose and hemipeptone into amido-acids, while the other, passing through antialbumose, halts at antipeptone."

We have two hypotheses: (I) Kühne's hypothesis of *cleavage into two coördinate hemi-* and *anti-* molecules; and (II) Moore's hypothesis of *cleavage, from the proteid molecule* of *subordinate, amido-acid molecules.* The reader remembers that in salivary digestion the starch molecule is subjected to a series of hydrolytic cleavages, but that these cleavages are not *coördinate.* In each cleavage a *subordinate* molecule maltose is split off from the carbohydrate molecule until the whole carbohydrate molecule is finally broken up into maltose molecules. According to Moore's hypothesis: "The different proteids, especially the proteoses, differ so little in chemical composition that the difference in their nature is probably due to a difference in atomic grouping. * * * Some of these groups are much more susceptible of decomposition than others. * * * Those albumoses which yield much amido-acid contain in their molecules more groups which are decomposable by trypsin. * * Those which yield much antipeptone contain less of these decomposable groups. * * In all cases that substance which we call antipeptone is the *remainder* after all of those groups which are attackable by trypsin have been removed in the form of amido-acids." The process which Moore outlines is in harmony with the facts and is analogous to ptyalin digestion. Moore's hypothesis presents no hypothetical substances; it utilizes only substances separable by chemical methods from all other substances.

The facts of peptic proteolysis may be summarized in the following table:

SERIES I.	SERIES II.	CHARACTERISTICS.
Native Proteid.	Native Proteid.	Responds to xanthoproteic test, to Millon's test. Is indiffusible.
Syntonin.	Syntonin.	Soluble in dilute acids, insoluble in water, indiffusible.
	Proto-proteose	Soluble in H_2O; precipitated by $MgSO_4$, NaCl or $(NH_4)_2SO_4$ in Sat. Sol. Diffusible.
Primary Proteoses.	Hetero-proteose	Soluble in dilute NaCl solution, precipitated by Sat. Sol. NaCl or $MgSO_4$ and $(NH_4)_2SO_4$. Diffusible.
Secondary Proteoses.	Deutero-proteoses.	Soluble in water. Precipitated by $(NH_4)_2SO_4$. Diffusible.
Peptones.	Peptones.	Soluble in water, not precipitated by $(NH_4)_2SO_4$. Diffusible.

3. FACTORS WHICH INFLUENCE GASTRIC DIGESTION.

1. **The Preparation of Food.**—Inasmuch as gastric digestion is confined to proteids it is now in order to determine the influence of cooking upon proteolysis. Proteids may be divided into two classes for the consideration of this subject.

(*a*) PROTEIDS WHICH ARE COAGULATED BY HEAT.—This class includes the native albumins and globulins. As already mentioned under cooking, the application of high temperatures to any of this class of proteids decreases the ease with which it may be digested. In the preparation of eggs (uncompounded); of clear lean meat, of beef juice or blood (serum albumin and serum-globulin) just as little heat should be applied as is possible to do and make a palatable dish.

(*b*) PROTEIDS WHICH ARE NOT COAGULATED BY HEAT—*Albuminoids.* *Collagen* is the sole representative of this class which is important here. Collagen enters into the formation of all of the connective tissues of the animal body. In preparing most cuts of meat one has to deal with a large proportion of connective tissue. If properly prepared it is digestible and nourishing, if not so prepared it is almost indigestible itself and its presence keeps the digestive juices from gaining proper access to the simple proteids and thus prolongs very greatly the period of their digestion. When connective tissue is subjected to heat in the presence of moisture the collagen becomes hydrated into gelatin. The meat is then easily masticated, the digestive juices readily penetrate it and the gelatin itself is readily digested.

2. **The Mastication of Food.**—Under mastication the importance of this process was urged.

3. **The Reaction of the Contents of the Stomach.**—From what appeared above it is evident that gastric digestion cannot proceed in an alkaline medium. The first step in the process being the formation of acid-albumin, it is important to determine what acids may serve the purpose.

(*a*) THE KIND OF ACID NECESSARY.—The hydrochloric acid of the gastric juice is nature's acid. Under certain conditions lactic acid appears in moderate quantities. Any conditions which lead to a decrease in the hydrochloric acid favor the appearance of lactic acid, a fermentation product. In peptic proteolysis *lactic acid may take the place of hydrochloric acid.* Several organic acids are taken with the food: *acetic acid*, in vinegar; *malic acid*, in rhubarb, strawberries, apples, etc.; *citric acid*, in lemons and oranges, and *tartaric acid*, in grapes. Any of these acids may supplement, or even replace, the hydrochloric acid in gastric digestion.

(*b*) THE AMOUNT OF ACID NECESSARY.—Experiment shows that though 0.3 per cent. is the strength of the hydrochloric acid in pure gastric juice, that is not the strength necessary for the formation of acid-albumin. The foods taken into the stomach dilute the acid very much, so that it is hardly likely that the acid of the stomach during digestion represents more than 0.1 per cent. of the whole contents of the stomach. Digestion proceeds rapidly in HCl of that strength. Just how strong the other acids should be is not determined. It is not likely that they could be effective in less than 0.1 per cent. strength. Experiment has shown that 0.1

per cent. to 0.4 per cent. represent average favorable limits with some variation in the lower limit for different organic acids. The presence of moderate quantities of organic acids probably exerts relatively little effect upon digestion. The tendency of many to use these acids very freely, together with the influence which the presence of other acids has upon the secretion of hydrochloric acid makes this question of importance to the clinician. If one were to drink a large quantity of lemonade at the beginning of a meal it is evident that the strong acid reaction of the stomach would greatly retard salivary digestion. It is also certain that it would decrease the secretion of hydrochloric acid. On the other hand, a moderate amount of any acid drink or food toward the end of the meal may serve an important purpose in supplementing the acid of the gastric juice.

4. **The Influence of Temperature.**—What was said of the influence of temperature upon salivary digestion applies equally to gastric digestion.

5. **The Influence of Dilution.**—Much has been said and written against the drinking of cold water with meals, and especially at the beginning of meals. There is more misconception regarding water than any other food. Without entering into a discussion of the details of the question, and without citing the numerous and reliable authorities, the author will briefly state a few of the fundamental facts regarding the relation of water to nutrition: (I) Water is a prime necessity to the animal body. Lack of sufficient water is just as certain to lead to a derangement of the nutrition of the body as is lack of sufficient solid food. Most people use too little water; few people use too much water. (II) The free use of water does not tend directly to the accumulation of fat. The statement that it does so is a fallacy which arises from these facts: The free use of water facilitates the processes of nutrition and economizes food by utilizing a greater proportion of it. Under such conditions any excess of food tends to be deposited as reserve material in the form of fat. The reasonable thing to do, if one wishes to decrease the tendency to accumulate fat, is not to induce a pathological condition by the decrease of the water; but to *simply decrease the fat-forming material, i. e., decrease the carbohydrates and fats.* (III) Cold water stimulates the free secretion of gastric juice. Cold water in moderate quantity at the beginning of a meal thus hastens the gastric digestion and makes more efficient the antiseptic action of the gastric juice. Recalling what was said regarding the relation of water and other diluents to salivary digestion it is evident that several of the factors which hasten and facilitate gastric digestion at the same time retard or stop salivary digestion. We have to choose between these two alternatives. Which process is the more important to the system?

The amylolytic enzyme of the pancreatic juice is much more active than is ptyalin. The conditions for digestion of starches are more favorable in the intestine than in the stomach.

By far the most important processes which take place in the stomach are: (I) The disinfection of the stomach contents by the hydrochloric acid; (II) the digestion of proteids. The prolonging of salivary digestion is of much less importance than either of these. The reasonable thing to do is to stimulate the secretion of gastric juice. *Water is, next to peptone, the most efficient agent in the stimulation of the secretion of gastric juice.*

6. **The Influence of the Movements of the Stomach.**—The movements of the stomach facilitate gastric digestion (I) by mixing the gastric juice with the food, and (II) by removing those portions already digested.

We shall find that movements of the stomach (to be discussed later) are *wholly involuntary.* If they are to be controlled or modified in character it must be through the influence of reflexes (*inherent reflexes*, which see). One may indirectly influence the rate of the heart by influencing the factors which control the heart. In the same way, to a smaller extent, perhaps, one may influence the movements of the stomach by influencing the factors which control the stomach musculature. Cannon ("The Movements of the Stomach," *American Journal of Physiology*, Vol. I., p. 359), after a series of observations on the influence of the emotions upon the movement of the stomach, thus summarizes his results: "The stomach movements are inhibited (actually stopped) whenever the cat shows signs of anxiety, rage or distress." That strong emotions inhibit the movements of the human stomach and thus retard gastric digestion is beyond doubt.

4. THE MOVEMENTS OF THE STOMACH.

The most recent and most valuable contribution to our knowledge of the movements of the stomach has been made by Cannon, cited above, who has worked under the inspiration of Prof. Bowditch, of Harvard. The *Röntgen Rays* were utilized in producing a series of sketches of the stomach in action. To make the contents of the stomach opaque to the rays subnitrate of bismuth was mixed with the food. A clear conception of the gastric movements and of the effect of these movements may be gotten by reproducing here some of Cannon's figures and quoting his summary:

(*a*) "The Stomach Consists of two physiologically distinct parts: the pyloric part and the fundus. Over the pyloric part, while food is present, constriction waves continually course toward the pylorus. The fundus is the active reservoir for the food and

Fig. 175.

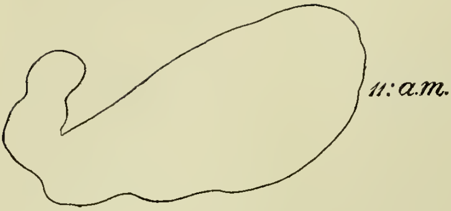


Fig. 176.

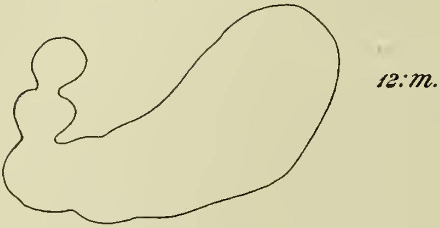


Fig. 177.

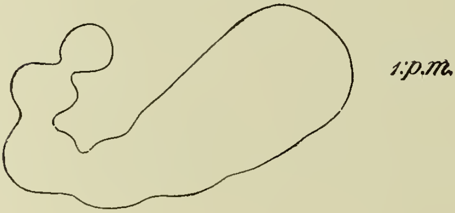


Fig. 178.

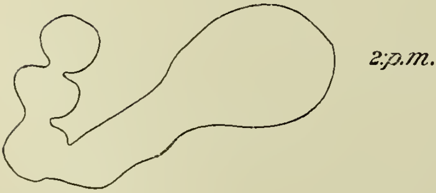


Fig. 179.

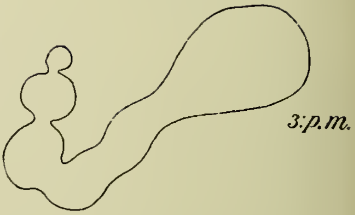


Fig. 180.

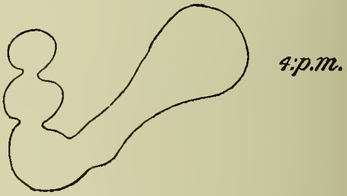


Fig. 181.

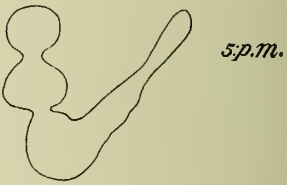
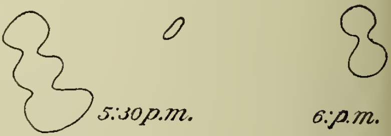


Fig. 182.



The movements of the stomach.

These figures present the "outlines of the shadow of the contents of the stomach cast on a fluorescent screen by the Röntgen ray. * * * They show the change in the appearance of the stomach at intervals of one hour from the time of eating until the stomach is nearly empty." (Cannon.)

squeezes out its contents gradually into the pyloric part." (Fig. 155.)

(*b*) "THE STOMACH IS EMPTIED by the formation between the fundus and the antrum of a tube (preantral portion) along which constrictions pass. (See Fig. 157.) The contents of the fundus are pressed into the tube and the tube and antrum slowly cleared of food by the waves of constriction."

(*c*) "THE FOOD IN THE PYLORIC PORTION is first pushed forward by the running wave, and then by pressure of the stomach wall is returned through the ring of constriction; thus the food is thoroughly mixed with gastric juice and is forced by an oscillating progress to the pylorus." (See Fig. 175 *et seq.*)

(*d*) "THE FOOD IN THE FUNDUS is not moved by peristalsis, and consequently it is not mixed with the gastric juice; salivary digestion can, therefore, be carried on in this region for a considerable period without being stopped by the acid gastric juice."

(*e*) "THE PYLORUS DOES NOT OPEN at the approach of every wave but only at irregular intervals. The arrival of a hard morsel causes the sphincter to open less frequently than normally, thus materially interfering with the passage of the already liquefied food."

(*f*) "SOLID FOOD REMAINS in the antrum to be rubbed by the constrictions until triturated, or to be softened by the gastric juice, or later it may be forced into the intestine in the solid state."

(*g*) "THE CONSTRICTION WAVES have, therefore, three functions; the *mixing*, *trituration* and *expulsion* of food."

5. VOMITING.

a. The Mechanism of Vomiting.

In discussing this subject one must differentiate between, (I) mild vomiting without nausea; and, (II) violent vomiting with nausea. Dogs and infants are likely to overload the stomach. The latter responds by a firm contraction of the pylorus or sphincter antri pylorici followed by a general contraction of the walls of the stomach, the result being a regurgitation of a part of the just swallowed food. That there is no nausea associated with this act is evidenced by the fact that the "dog returneth to his vomit," eating the food a second time; if the dog were nauseated he would not do that. But in adult man, "the act of vomiting is generally preceded by a feeling of nausea, and usually there is a rush of saliva into the mouth, caused by a reflex stimulation through the afferent fibers of the gastric vagus and the efferent chorda tympani" (Stirling). After this a deep inspiration is taken and the glottis closed so that the diaphragm is firmly pressed down upon the abdominal contents; and it is kept contracted while a violent contraction of the abdominal muscles forcibly compresses the stomach, whose contents are ejected. This movement is so sudden that the sluggishly contracting involuntary muscles of the stomach walls do not have time to assist.

b. The Influence of the Nervous System upon Vomiting.

(*a*) THE EFFERENT IMPULSES pass to the pyloric sphincters, the diaphragm, the abdominal muscles and the muscles of the larynx and pharynx through the vagus, phrenic, lower intercostals and the superior maxillary division of the V.

(*b*) THE VOMITING CENTER, though not definitely located, exists somewhere in the medulla. The muscles which are most active in vomiting are the respiratory muscles. The vomiting center must be associated with the respiratory center; it may be identical with the respiratory center in whole or in part, or it may, under particular conditions, simply dominate the respiratory center. The vomiting center, indefinite though it is anatomically, is definitely influenced by certain different impulses.

(*c*) THE AFFERENT IMPULSES reach the medullar center through: (I) the vagus, which is stimulated by any gastric irritant; (II) the trigeminus and the glosso-pharyngeal, which is stimulated when the uvula and fauces are tickled; (III) the afferent nerves supplying the urogenital tract, stimulated by irritation of that tract, *e. g.*, uterine nerves stimulated during pregnancy; (IV) finally, impulses may reach the vomiting center from the cerebrum or cerebellum which may induce vomiting. These impulses may be caused by certain pathological conditions, or may be induced through the cerebrum by certain sights, odors or taste, or may be induced purely psychically through the memory of certain experiences which were associated with nausea. Disturbances of equilibrium may through this same *central* influence induce vomiting.

Drugs which induce vomiting are called emetics.

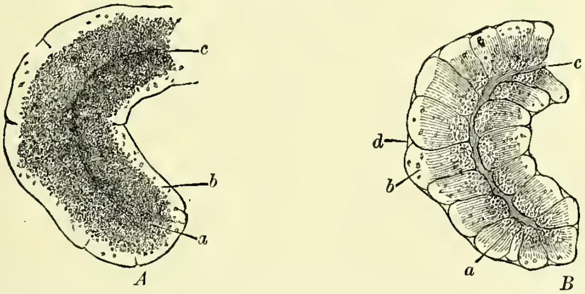
C. INTESTINAL DIGESTION.

1. THE DIGESTIVE FLUIDS.

a. The Secretion of Pancreatic Juice.

The pancreas represents the compound tubular type of glands The general arrangement of its ducts and tubular alveoli is shown in Fig. 161 under *Secretion.* The structural changes which take place in the cells of the pancreas during secretion are quite like those which are observed in the salivary glands during their activity, and these changes have the same significance. The accompanying figure (Fig. 183) shows the principal characteristic of these changes. During the resting stage the cells become loaded with zymogen granules, and their outlines are less clearly seen. After a period of secretion the granules become much less numerous, striæ appear in the cytoplasm, the unmodified cytoplasm is relatively much more abundant. The appearances justify the conclusion that parts of the secretion—the ferments—are formed from the granules ; that these granules become exhausted during secretion and are formed during rest at the expense of the cytoplasm. The cytoplasm, in its turn, is replenished during the secretory activity of the gland, the cells apparently seizing the opportunity when the blood supply is abundant to secure the needed nutriment. During the resting period the granules are formed at the expense of the cytoplasm. The secretion of pancreatic juice varies with the phase of digestion, beginning soon after a meal and reaching a maximum (in the dog), from one to three hours after the meal and gradually decreasing as digestion progresses. This relation of pancreatic secretion to conditions in the alimentary canal makes it certain that the secretion is a reflex act.

Fig. 183.



Part of an alveolus of the rabbit's pancreas. *A*, at rest ; *B*, after active secretion. *a*, the inner granular zone, which in *A* is larger and more closely studded with fine granules than in *B*, in which the granules are fewer and coarser ; *b*, the outer transparent zone, small in *A*, larger in *B*, and in the latter marked with faint striæ ; *c*, the lumen, very obvious in *B*, but indistinct in *A* ; *d*, an indentation at the junction of two cells, only seen in *B*. (From Schaefer after Foster and Kühne.)

The experiments of Dolinsky (*Archives des Sci. biologique*, St. Petersburg, 1895, Vol. III., p. 399) show that this reflex act is stimulated especially by the presence of acid in the alimentary tract ; *i. e.*, anything which will stimulate the flow of gastric juice will in turn stimulate the flow of pancreatic juice. Alkalies in the stomach diminish the secretion of pancreatic juice. Pawlow has shown that the vagus contains the secretory nerves of the pancreas. Extirpation of the pancreas is followed by diabetes.

b. The Composition of the Pancreatic Juice.

The sensitiveness of the pancreas to any operative procedures makes it difficult to get a normal secretion from a fistula. The establishment of the fistula is followed by inflammatory changes. Before these changes occur a secretion may be caught which is called temporary. After the inflammatory changes have subsided the secretion approaches the normal qualitatively though it contains a much smaller proportion of solids.

The following table gives two analyses by Carl Schmidt (Quoted by Maly in Hermann's *Handbuch d. Physiol.*, Bd. V. (2), S. 189) from temporary and permanent fistulæ; also an analysis by Zawadsky (*Centralbl. f. Physiol.*, 1891, Bd. V., S. 179) of normal human pancreatic juice:

CHEMICAL COMPOSITION OF PANCREATIC JUICE.

CONSTITUENTS.	FROM A TEMPORARY FISTULA (DOG).	FROM A PERMANENT FISTULA (DOG .	HUMAN PANC. JUICE.
WATER.	90.08	97.68	86.405
SOLIDS:	9.92	2.32	13.595
Organic: Enzymes, etc.	9.04	1.64	13.251
Inorganic.	0.88	0.68	0.344
Na_2CO_3	0.06	0.33	
NaCl	0.74	0.25	
KCl	trace.	0.09	
Ca, Mg and Na phosphates.	0.08	0.01	

The pancreatic juice contains several important constituents:

1. **Enzymes.**— (I) An amylolytic enzyme.—*Amylopsin.*
(II) A proteolytic enzyme.—*Trypsin.*
(III) A fat-splitting enzyme.—*Steapsin.*
(IV) A milk-curdling enzyme.

2. **Alkaline Salts**: Na_2CO_3, and Na_3PO_4.

The influence of the salts is to make the alkalinity of the pancreatic juice equal to 0.2–0.4 per cent. of NaOH.

c. The Composition of the Succus Entericus.

This fluid is secreted by the crypts of Lieberkühn. The secretion is caught by making a fistula. The Vella-Thiry fistula is formed "by cutting across the intestine at two places, 10–30 cm. apart, without interfering with the blood supply, restoring the continuity of the intestine, * * * stitching both ends of the isolated piece to the abdominal wall, leaving a double fistulous opening" (Moore). Fluid caught from such a fistula is limpid, opalescent, has a specific gravity ranging from 1.010 to 1.014, an alkalinity of nearly 0.5 per cent. NaOH; it contains proteids, and coagulates on standing. It contains 2 to 3 per cent. of solids, of which 0.7 per cent. to 0.9 per cent. is ash. Human succus entericus from the ileum near the ileo-cæcal valve[1] contained a much smaller proportion of solids, and had a Sp. Gr. 1.0069.

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[1] Tabby and Manning, *Guy's Hosp. Rep.*, London, 1891, Vol. XLVIII., p. 277. Quoted by Moore.

The most important constituents of the succus entericus are : (*a*) An enzyme : *Invertine.* (*b*) Alkaline salts : Na_2CO_3, etc.

d. Composition of the Bile.

The consideration of the bile in its relation to metabolism will be taken up later. It will be sufficient to summarize its composition here, and to discuss under digestion only those features which especially influence digestion.

TABLE SHOWING THE COMPOSITION OF HUMAN BILE.

CONSTITUENTS.	FROM GALL-BLADDER.*	FROM FISTULA.**
WATER.	89.81	98.72
SOLIDS.	10.19	1.28
Organic :		
Glycocholate of sodium.	5.65	0.16
Taurocholate of sodium.		0.06
Cholesterin, lecithin, fats and soaps.	3.09	0.04
Mucin, pigment, epithelium, etc.	1.45	0.15
Inorganic salts :	0.63	0.84
Na_2CO_3, Na_2HPO_4		

Note that the bile contains no ferment. Its most important constituents are the Na_2CO_3, the Na_2HPO_4 and the glycocholate and taurocholate of sodium.

2. THE CHEMISTRY OF INTESTINAL DIGESTION.

a. The Action of the Pancreatic Juice.

The pancreatic juice is active chemically through its alkaline salts and its enzymes. The alkaline salts of the intestinal fluids neutralize the acids which enter the duodenum from the stomach and, in the typical case, make the intestinal contents distinctly alkaline. In an alkaline medium all of the enzymes act more vigorously than in a neutral or faintly acid medium.

1. **The Amylolytic Enzyme—Amylopsin.**—This enzyme is practically identical with ptyalin in all its properties except that its action is very much more rapid. Like ptyalin it acts best in an alkaline medium, and like that enzyme it changes starch to maltose. In the discussion of salivary digestion it cannot have escaped the attention of the reader that the ptyalin, under the most favorable circumstances, digests only a small proportion of the starch. Due to the imperfect cooking to which starchy foods are so frequently subjected, to the imperfect mastication and insalivation which are so prevalent, and to the almost universal dilution of the contents of the stomach with liquid foods or drinks, the action of the ptyalin is reduced to a most unimportant rôle. It is to the amylolytic enzyme of the pancreatic juice that we must look for the digestion of the amyloses.

The conditions under which this enzyme acts are most favorable, the temperature, the reaction, the degree of dilution, the trituration of the foods by the stomach are all favorable to rapid action of the amylopsin. Even raw starch is readily digested *in vitro* by the amylopsin. The conditions to which incompletely cooked starch is subjected in the stomach probably make it more easily digestible than is the raw starch used in laboratory experiments.

One may thus sum up the action of amylopsin: (I) It acts upon raw or cooked starch causing a series of hydrolytic cleavages identical with those caused by ptyalin (which see). The hydrolysis is probably complete, resulting finally in producing *maltose, from starch.* (II) It acts upon the dextrines which have been previously formed by ptyalin; viz.: amylodextrin, erythrodextrin, the achroödextrins α, β, and γ, completing the hydrolytic changes already begun; thus *producing maltose from dextrines.* (III) It acts upon *glycogen changing it to maltose* through a series of cleavages parallel to or identical with those observed in the amylolytic digestion of starch.[1]

2. **The Proteolytic Enzyme—Trypsin.**—The proteid-digesting enzyme of the pancreatic juice differs from that of the gastric juice in requiring an alkaline medium instead of an acid medium for its activity.

The first step of tryptic proteolysis is the formation of *alkali-albumin.* This at once initiates a series of hydrolytic changes which though parallel to the changes of peptic proteolysis are not identical with them. The proteoses formed cannot be chemically separated into primary and secondary proteoses. There is, therefore, no protoproteose and no heteroproteose. *Deuteroproteoses* are formed passing in several slightly varied forms but all of them fulfilling the requirements of deuteroproteose or deuteroalbumose. The deuteroproteose formed in tryptic proteolysis is apparently identical in its response to chemical reactions with the deuteroproteose formed in peptic proteolysis. Neumeister finds that there are several deuteroproteoses formed in tryptic digestion, and that all of them yield on further cleavage both peptone and amido-acids. The deuteroproteose of peptic proteolysis apparently gives rise to *two coördinate peptones* (whose mixture is called amphopeptone), one of which (the hypothetical hemipeptone) may be decomposed under the influence of trypsin into a series of amido-acids while the other (antipeptone) can not be so decomposed. The deuteroproteose of tryptic proteolysis gives rise to peptone and to the series of amido-acids, *i. e.*, there is experimental evidence of a *subordinate hydrolytic cleavage* of deuteroproteose but no experimental evidence of a *coördinate cleavage* into two peptones. In the terms of those who contend for a coördinate cleavage one may say that the deuteroproteose of tryptic digestion is *anti-deuteroproteose*, and the peptone is *antipeptone*, while the *hemi*-group wherever formed in the proteolysis is instantly decomposed into amido-acids.

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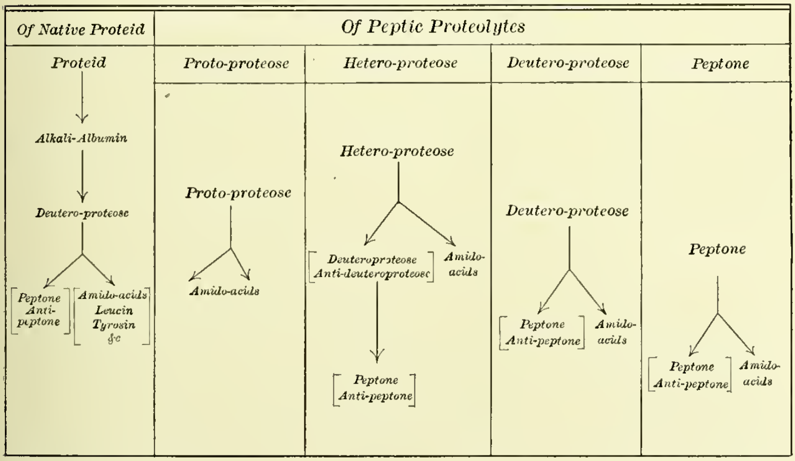
[1] The fact that the amylolytic ferment is absent from the pancreatic juice of infants makes it evident that they are not prepared by nature for starchy foods. Milk is nature's food for mammalian young, as witness all indications both in the mother and offspring. In the young mammal there are: (I) abundant and active milk-curdling enzymes; (II) Proteolytic enzymes; (III) a fat-splitting enzyme, and (IV) an inverting enzyme.

The action of trypsin upon native proteids and upon peptic proteolytes may be thus summarized:

TABLE OF TRYPTIC PROTEOLYSIS.



The peptone (antipeptone) of tryptic digestion is the form in which most of the proteid foodstuffs are absorbed. From this substance and from some sulphur-containing compound, protoplasm and other higher proteids seem to be built up by a process of anabolism. It is important to determine the constitution of the substance. There is strong evidence that it is identical with Siegfried's *Fleischsäure* (*Archiv f. Anat. u. Physiol.*, Leipzig, 1894, S. 401; *Zeitch. f. Physiol. Chem.*, Strassburg, 1896, Bd. XXI., S. 360).

Both compounds react the same in the biuret test; both fail to respond to Millon's reagent; both are very hygroscopic; both yield, on decomposition with hydrochloric acid, lysin and lysatinin. Fleischsäure has been obtained directly from the products of advanced tryptic digestion. Both of the bodies under consideration are easily soluble in water. From a hot alcoholic solution Fleischsäure crystallizes in minute crystals. Siegfried has determined the formula of Fleischsäure to be $C_{10}H_{15}N_3O_5$ (mol. wt. 257), Sjöquist (quoted by Moore from *Skand. Arch. f. Physiol.*, Leipzig, 1896, Bd. V., S. 277) determined the molecular weight of antipeptone (cryoscopic method) to be 250. In the light of these facts it seems certain that antipeptone and Fleischsäure are either identical or closely allied and that the quantitative formula for the two is probably represented in the determined formula for Fleischsäure.

Frequent reference has been made to the amido-acids formed in tryptic proteolysis and to organic bases (lysin, lysatin, etc.) formed in the hydrolytic decomposition of proteids. The composition of these bodies may be briefly summarized.

(*a*) Lucein or Isobutyl-*α*-amido-acetic acid.

$$(CH_3)_2—CH—CH_2—CH{\cdot}NH_2—COOH.$$

The proteids yield, on decomposition the following per cents. of leucin: Egg albumin, 22.6 per cent.; casein, 19.1 per cent.; muscle, 18 per cent.; vegetable albumin, 17.3 per cent.; fibrin, 7.9 per cent. in digestion, 14 per cent. in decomposition with H_2SO_4; gelatin, 1.5 per cent. to 2 per cent. (Maly).

(*b*) Tyrosin or p-oxyphenyl-*α*-amido-propionic acid.

$$C_6H_4{\cdot}OH—CH_2—CHNH_2—COOH.$$

In decomposition of various proteids the largest proportion of tyrosin was obtained from casein (4.1 per cent.), followed in turn by fibrin (3.3 per cent.) egg albumin or vegetable albumin, and muscle (1 per cent.), while gelatin yielded none.[1]

It must be remembered that these results represent the greatest quantity of tyrosin or leucin which it is possible to split off from the proteids mentioned. The amount actually formed in digestion is probably much smaller.

(*c*) Butalanin or Amido-valerianic acid.

$$(CH_3)_2—CH—CH{\cdot}NH_2—COOH.$$

(*d*) Aspartic Acid or Amido-succinic acid.

$$COOH—CH_2—CH{\cdot}NH_2—COOH.$$

(*e*) Glutamic Acid or Amido-pyrotartaric acid.

$$COOH—CH_2—CH_2—CH{\cdot}NH_2—COOH.$$

Besides these amido-acids certain bases which are formed in tryptic digestion as well as in decomposition of proteids.

(*f*) Lysin or *α*-*ε*-diamido-caproic acid.

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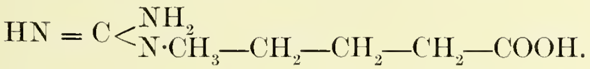
[1] Quoted from Maly in Hermann's Handbuch, Bd. V. (2), S. 209.

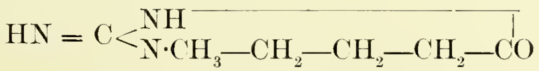
$$CH_2\cdot NH_2—(CH_2)_3—CH\cdot NH_2—COOH.$$

(*g*) Lysatin (or methyl guanidin butyric acid).



$$HN = C<\begin{matrix}NH_2\\ N\cdot CH_3—CH_2—CH_2—CH_2—COOH.\end{matrix}$$

(*h*) Lysatinin.



$$HN = C<\begin{matrix}NH\text{———————————}\,|\\ N\cdot CH_3—CH_2—CH_2—CH_2—CO\end{matrix}$$

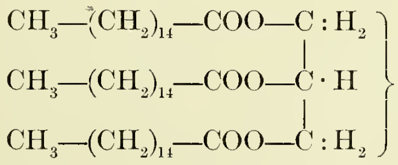
Lysatin belongs to the same series with kreatin, and lysatinin is homologous with kreatinin, *i. e.*, it is lysatin minus H_2O.

Ammonia (NH_3) is formed in both tryptic digestion and decomposition.

3. **The Fat-Splitting Enzyme—Steapsin.**—Fats are not changed chemically in any of the digestive processes which take place before they reach the small intestine. Adipose tissue, consisting of collagen and fat, is broken up in the stomach by the peptic digestion of the collagen (or gelatin), which releases the fat. Animal fat is fluid at the temperature of the animal body.

The released and fluid fat is mixed with the acid chyme in the form of small globules and passes into the duodenum. The alkaline salts of the pancreatic juice and bile neutralize all free hydrochloric acid and change the reaction to neutral or alkaline in the duodenum.

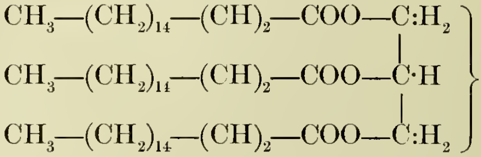
A simple fat, as tripalmitin, is a combination of three fatty acid molecules with propenyl, the glycerol radical. The general structural formula of the fatty acids of the primary monatomic alcohol series is: $CH_3—(CH_2)_{n-2}—COOH$. The formula of palmitic acid, the 16th member of the series, is: $CH_3—(CH_2)_{14}—COOH$; of stearic acid the 18th member; $CH_3—(CH_2)_{16}—COOH$. Tripalmitin has the following structural and quantitative formulæ:



$$\left.\begin{matrix}CH_3—(CH_2)_{14}—COO—C:H_2\\ |\\ CH_3—(CH_2)_{14}—COO—C\cdot H\\ |\\ CH_3—(CH_2)_{14}—COO—C:H_2\end{matrix}\right\}$$

or $[CH_3—(CH_2)_{14}—COO]_3—C_3H_5$, or $(C_{16}H_{31}O_2)_3\cdot C_3H_5$.

Oleic acid belongs to the triatomic alcohol series whose acids possess the following general formula: $CH_3—(CH_2)_{n-4}—(CH)_2—COOH$. Oleic acid is the 18th member of the series and has the formulæ: $CH_3—(CH_2)_{14}—(CH)_2—COOH$ or $C_{18}H_{34}O_2$. Triolein has the constitution indicated in the formula:



$$\left.\begin{array}{l} CH_3—(CH_2)_{14}—(CH)_2—COO—C{:}H_2 \\ \qquad\qquad\qquad\qquad\qquad\qquad\quad | \\ CH_3—(CH_2)_{14}—(CH)_2—COO—C{\cdot}H \\ \qquad\qquad\qquad\qquad\qquad\qquad\quad | \\ CH_3—(CH_2)_{14}—(CH)_2—COO—C{:}H_2 \end{array}\right\}$$

or $$[CH_3—(CH_2)_{14}—(CH)_2—COO]_3{\cdot}C_3H_5$$

Animal fat is a mixture of tri-palmitin, tristearin, and triolein in various proportions. Certain fats and oils, especially vegetable oils, have various other members of the fatty acid or oleic acid series.

The task which presents itself now is to find the effect of steapsin upon these compounds. Let tri-palmitin be taken as a type. Steapsin brings about a hydrolytic cleavage of the molecule into its constituents:

$$[CH_3—(CH_2)_{14}—COO]_3C_3H_5 + 3H_2O =$$
$$C_3H_5{\cdot}(OH)_3 + 3CH_3—(CH_2)_{14}—COOH$$

Tri-palmitin + 3 water = glycerol + 3 palmitic acid.

This hydrolytic cleavage of the fats leads to an accumulation of glycerin and of various fatty acids in the intestine. The presence of the fatty acids induces, or facilitates three important changes in the contents of the small intestine.

(*a*) EMULSIFICATION. Oil is emulsified when it is separated into minute globules which are suspended in the medium and remain separate. If the globules remain separate indefinitely showing no tendency to coalesce the emulsion is said to be *permanent;* while in a *temporary* emulsion the oil globules gradually coalesce and rise to the top of the medium. Emulsions may be classified also on the basis of their formation whether *mechanical* or *chemical.* If an oil be vigorously shaken with a viscous menstruum, such as egg-albumin, or a gum or sugar syrup, the division of the oil may be as fine and the persistence of the emulsion as permanent as in the case of a chemical emulsion. The success of this mechanical emulsion will depend largely upon the vigor and the time of the mechanical agitation. A chemical, also called *spontaneous,* emulsion is produced when the conditions are favorable for the formation of soaps in the fat. Under these conditions a fat or oil will very soon be transformed into a permanent emulsion without the help of shaking, without mechanical aid, though the process is hurried if the materials are shaken or stirred. Both fatty acids and alkalies are present; soap is formed and the contents of the small intestine are mixed by the peristaltic action of the intestinal walls. The conditions are thus favorable for both chemical and mechanical action.

(*b*) Saponification. As has already been stated the conditions favorable to the formation of soap exist in the small intestine. The pancreatic secretion, the bile, and the succus entericus all contain Na_2CO_3. When a fatty acid and Na_2CO_3 come together a sodium soap is instantly formed :

$$2\,CH_3\text{—}(CH_2)_{14}\text{—}COOH + Na_2CO_3 = \\ H_2O + CO_2 + 2\,CH_3\text{—}(CH_2)_{14}\text{—}COONa$$

2 Palmitic acid + sodium carbonate = $H_2O + CO_2 + 2$ soap.

(*c*) Reaction. The influence of steapsin upon the reaction in the small intestine has only recently come to the attention of physiologists. As stated above, the first effect of the alkaline secretions of the small intestine is to neutralize all the free acid of the chyme, and to make the contents of the small intestine neutral or alkaline. The second effect is to liberate from the fats a series of fatty acids, and from Na_2CO_3, carbonic acid gas. These acids though weak suffice to give the contents of the small intestine an acid reaction. But what is of very great importance to the organism these particular acids do not interfere with the digestive processes going on in the small intestine.

4. **The Milk-Curdling Enzymes.**—Pancreatic juice or an aqueous extract of fresh pancreas has the power to curdle milk. That the pancreatic juice has the opportunity to curdle milk, even when a full meal is made of that food, is hardly likely.

b. The Action of the Bile.

This secretion contains no enzyme. Its action is, however, very important when taken in connection with the action of the fat-splitting enzyme of the pancreatic juice. The glycerine liberated by the hydrolytic cleavage of the fats is soluble in water and is probably absorbed readily as glycerine ; the fatty acids liberated in the process are insoluble in water and have a melting point considerably above the temperature of the blood (palmitin at 62° C., stearin 69° C.). If they are not dissolved they would pass through the alimentary canal unabsorbed. A part of the fatty acids is combined as soap which is soluble. Of the Na_2CO_3 required for this process the bile furnishes much the greater part. Any fatty acid not combined in soap is dissolved in the glycocholates of sodium and of potassium. When the bile secretion is diverted from the alimentary canal through a fistula a large part of the ingested fat $\frac{1}{3}$ to $\frac{2}{3}$ appears in the fæces as fatty acids. Munk (*Virchow's Archiv*, 1890, Bd.

CXXII., S. 302, quoted from Moore) found that the absorption of fats of high melting point suffered more than that of fats of low melting point. Now, the fats of high melting point contain a preponderance of stearin whose acid (stearic acid) has a high melting point (69° C.) and thus resists other intestinal solvents of fatty acids.

Another most important property of the bile salts is their ability to *dissolve the soaps of the alkaline earths.* Most drinking water contains calcium and magnesium salts in solution. These salts combine at once with fatty acids to make calcium or magnesium soaps, or they displace Na from the soluble soaps already formed. These soaps of Ca and Mg are insoluble in water and but for the presence of the glycocholate of Na and K would pass out of the alimentary canal unabsorbed (Neumeister, *Lehrbuch der physiol. Chemie*, Jena, 1893).

One may summarize as follows the action of the bile in the digestive process:

(*α*) It assists in the emulsification of fats.

(*β*) It assists in the saponification of fats.

(*γ*) Its glycocholates and taurocholates assist in the solution of fatty acids.

(*δ*) Its salts in solution dissolve the soaps of the alkaline earths (insoluble in water).

(*ε*) Bile stimulates the contraction of the muscularis mucosa of the villi, thus accelerating the absorption.

(*ζ*) It acts as a "natural laxative" through (I) lubrication of the fæces; (II) stimulation of the muscular action in peristalsis.

(*η*) It diminishes putrefaction in the large intestine.

c. The Action of Succus Entericus.

Reference has already been made to the fact that the Na_2CO_3, which makes 0.25 per cent. to .5 per cent. of the intestinal juice, assists the pancreatic juice and bile in the emulsification and saponification of fats.

The most important constituent of the intestinal juice is the inverting enzyme, *Invertin.* This enzyme acts upon disaccharids, and through hydrolytic cleavage resolves them into two coördinate monosaccharid molecules. The amylolytic enzymes of the saliva and pancreatic juice change starch to maltose, a disaccharid. The sugar of milk is lactose, a disaccharid. An important article of diet is cane sugar, another disaccharid. All of these disaccharids possess the quantitative formula $C_{12}H_{22}O_{11}$.

Experiment has determined that none of these disaccharids appear in the blood. Only monosaccharids appear in the blood. The change from disaccharids to monosaccharids must take place before the sugar is discharged into the portal blood. The intestinal canal possesses in the *invertin* an enzyme capable of inducing the required changes :

(*a*) Maltose + H_2O + invertin = invertin + 2 dextrose.
$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O$.

(*b*) Lactose + water = dextrose + galactose.
$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$.

(*c*) Saccharose + water = dextrose + levulose.
$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$.

For the structural formulæ the reader is referred to the introduction to this chapter.

d. The Digestion of Milk: A Summary.

Milk is a perfect food (for composition see foods). Its carbohydrate *lactose* is already in solution. Its proteids are lact-albumin and caseinogen. Its fat is a composite of many simple fats, such as tri-olein, tri-palmitin and tri-stearin, with lower members of the palmitin series: the triglycerides of butyric (4th in the series); caproic (6th); caprilic (8th); capric (10th), and myristic (14th), acids. All of these lower members are present in very small and variable quantities. To their variation is due the various flavors of butter. Small quantities of lecithin and cholesterin are also present.

Milk is not acted upon by any constituent of the saliva. In the stomach it is first *curdled* by the action of the enzyme *rennin*. The curdling of milk consists in the coagulation of the caseinogen; after coagulation the caseinogen is called *casein*. The *casein* and the lact-albumin undergo the typical proteid digestion. The proteid pellicles which surround the oil globules are digested off and the oil escapes. After passing into the small intestine the digestion of the milk proteids is completed by the trypsin; the fats are acted upon by the steapsin forming an emulsion, and a long series of soaps, and free fatty acids. The lecithin is broken up into its constituents: For each lecithin molecule: (I) two fatty acid molecules, (II) glycero-phosphoric acid (III) cholin.[1]

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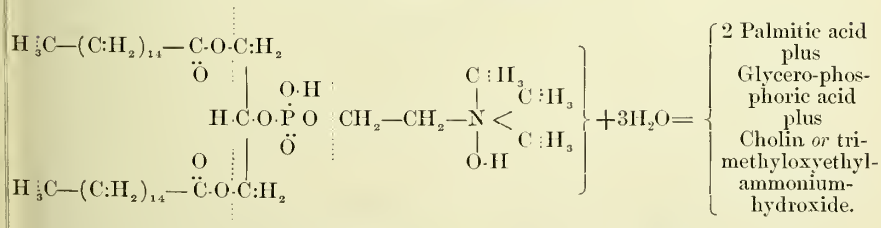
[1] Dipalmitic lecithin has the following structural formula :



The dotted lines indicate where the cleavage of the molecule takes place.

The lactose of the milk undergoes hydrolytic cleavage into dextrose and galactose.

3. FACTORS WHICH INFLUENCE INTESTINAL DIGESTION.

Such factors as cooking, mastication, and temperature have little direct influence upon intestinal digestion. Even the indirect influence is slight because the pancreatic juice can digest raw starch; the stomach retains the food until the imperfections of mastication are largely corrected; and its sojourn in the stomach certainly gives it the temperature of the body. There are three important factors yet to consider:

a. The Influence of Bacteria upon Intestinal Digestion.

"The food in the alimentary canal is acted upon, not only by the digestive secretions and their enzymes, but to a greater or less extent by certain bacteria, which are never entirely absent, although the amount of their action varies greatly under healthy conditions, with the nature of the food and the class of the animal. Under abnormal conditions the growth of these organisms may be greatly increased, and nutrition be seriously impaired *by the turning to their own uses the products of normal digestion*, and leaving, for the service of the animal, only degradation products inadequate or wholly unsuited for the purposes of its metabolism." (Moore.)

The effect of cooking and of the HCl of the gastric digestion is to practically free the chyme which enters the duodenum of all or nearly all bacterial life. We may look upon the bacteria of the intestinal tract as *parasites* introduced with the food and thriving only moderately when all of the conditions are normal. When the digestion is deranged the conditions may be favorable to the excessive development of various bacteria (organized ferments) whose food is robbed from the host and whose excreta may be extremely deleterious to the host. It has been contended that these parasites are "*beneficial*"; a similar contention might be made in behalf of certain vermin (!) *Parasitism is not beneficial.*

Nuttall and Thierfelder (*Zeitsch. f. physiol. Chemie*, 1895, Bd. XXI., S. 109) have demonstrated that young animals with sterile alimentary tract, sterile air and sterile food grow just as well as the control animals under the usual conditions. This applies as well for vegetable foods as for animal foods. Animals live and thrive in spite of their bacterial parasites and not because of them.

The action of bacteria may be discussed in its relation to different parts of the alimentary tract, and in its relation to different foodstuffs.

1. **The Action of Bacteria in Different Parts of the Alimentary Canal.**—(*a*) BACTERIA OF THE MOUTH have no influ-

ence upon intestinal digestion, though they may menace the teeth of the animal.

(*b*) BACTERIA OF THE STOMACH are introduced with the food and, as mentioned above, are usually destroyed by the HCl when that acid is sufficiently strong (0.2 per cent. to 0.3 per cent.). When the HCl is very weak, much delayed in secretion or wholly absent the development of *Bacterium lactis* and various fermentive and putrefactive forms is favored. In the case of *B. lactis* one might make an exception to the statement made above that bacteria and their excreta are not beneficial. Peptic digestion can only proceed in the presence of an acid. Lactic acid can take the place of HCl in forming acid albumin or syntonin. In the absence of HCl lactic acid, the excreta of *B. lactis* may be advantageous to the system.

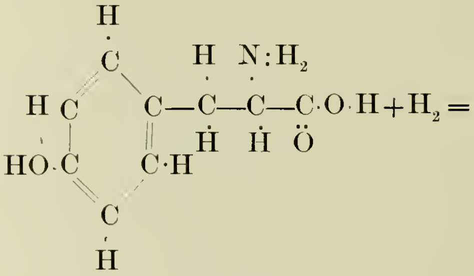
(*c*) BACTERIA OF THE SMALL INTESTINE.—The acid reaction of the chyme representing free HCl and acid albumin is neutralized and replaced with an acid reaction due to the accumulation of organic acids. At first these organic acids are fatty acids released by steapsin from neutral fats; these are, however, absorbed as absorption progresses; the acid reaction arising from this source will tend to decrease. But it has been observed (Macfadyen, Nencki, Sieber—*Arch. f. Exp. Path. u. Pharmacol.*), that the acid reaction usually found at the lower end of the ileum in man is due principally to *acetic acid*, with only traces of fatty and other acids. It seems likely that, in the small intestine, the acidity due to fatty acids is replaced from above downwards by acidity due to fermentation of carbohydrates. Moore and Rockwood (*Jour. Physiol.*, 1897, Vol. XXI., p. 373), in a very extended and recent series of observations upon the dog, cat, white rat, guinea-pig and rabbit, conclude: (I) "The reaction is not normally acid throughout the entire length of the small intestine, and the alkalinity increases in passing down the intestine." (II) "The presence of fat in the food causes in carnivora an acid reaction which persists until the lower third of the intestine is reached." (III) "The alkalinity is much greater in herbivora than in carnivora; * * also, in carnivora the alkalinity is markedly increased by carbohydrate food." (IV) "It is probable that in the animals observed any extensive bacterial decomposition of carbohydrates that may occur takes place in the large intestine." (Quoted from Moore.)

(*d*) BACTERIA OF THE LARGE INTESTINE.—In this segment of the alimentary canal the reaction is conceded by all to be *alkaline*, due to the neutralization of any acid entering the cæcum by the distinctly alkaline secretions of the mucous membrane. In the large intestine profound changes take place under the influence of putrefactive bacteria. The proteids are especially attacked in this segment of the canal, the acid reaction of the small intestine protecting them normally from putrefactive changes in that portion of the canal.

2. **The Action of Bacteria in Relation to Different Foodstuffs.** —(*a*) BACTERIAL ACTION ON CARBOHYDRATES consists (I) in the fermentation of the sugars with the formation of ethyl alcohol, acetic, lactic, butyric, and succinic acids, with the liberation of CO_2 and H; (II) in the decomposition of cellulose with the formation of marsh gas (CH_4) and CO_2; (III) in the decomposition of starch with products similar to (I). The fermentation and decomposition of carbohydrates begins in the small intestine and progresses with increasing activity through the cæcum, then with decreasing activity to the rectum.

(*b*) BACTERIAL ACTION ON PROTEIDS seems to be inhibited by the acid reaction of the small intestine. As soon as the contents of the alimentary tract become alkaline the decomposition of proteids is facilitated. There are two series of products formed during the putrefaction of proteids and the proteolytes. The members of the first series are derived from tyrosin in the following manner:

(Baumann, *Berich. d. deutsch. chem. Gesell.*, 1879, Bd. 12, S. 1450.)



$$NH_3+C_6H_4·OH—(CH_2)_2—COOH.$$

Tryosin or *p*-oxyphenyl-amido-propionic acid $+H_2=$

$$NH_3+\begin{cases} p\text{-hydrocumaric acid or} \\ p\text{-oxyphenyl-propionic acid.} \end{cases}$$

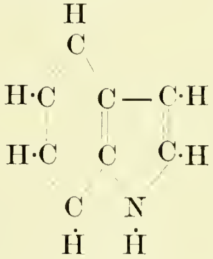
p-Hydrocumaric acid parts with CO_2 and becomes *p*-ethylphenol ($C_6H_4·OH—C_2H_5$) which has not, however, been found in the intestine, though it occurs in experiments *in vitro*, *p*-ethylphenol next becomes oxidized (+3O) to *p*-oxyphenyl-acetic acid. This in turn gives up CO_2 and becomes *p*-cresol (*p*-methyl phenol) which is again oxidized to *p*-oxybenzoic acid—not yet found in the intestine.

Oxybenzoic acid gives up CO_2 and forms phenol:

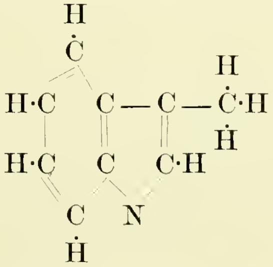
$$C_6H_4{\cdot}OH{-}COOH = CO_2 + C_6H_5{\cdot}OH$$
$$p\text{-oxybenzoic acid} = CO_2 + \text{phenol.}$$

The second series of products is less understood.

Indol has the following structure:



Skatol or Methyl-indol has the following structure:



Both of these bodies are soluble in water, from which solution they crystallize in small scales. Both are in part absorbed and in part passed out with the fæces.

b. The Influence of Cellulose upon Intestinal Digestion.

In the case of herbivora it has been demonstrated by Bunge [*Physiologische Chemie*, 1894, S. 75] that cellulose is important not as a nutrient but "in giving bulk and looseness to the food and in mechanically inducing peristalsis by irritation of the mucous membrane." To the herbivora it is indispensable, to omnivora like man it is advantageous in moderate quantities, to carnivora it has no advantages. Herbivora digest 60–70 per cent. of it, man, 4–60 per cent. according to the condition of the cellulose. Under the influence of bacteria it is subjected to a hydrolytic cleavage represented in the following equations:

$$[C_6H_{10}O_5 + H_2O = 3CO_2 + 3CH_4]_n$$

The reaction is varied by the production also of acetic, propionic, butyric, and valerianic acids.

4. THE REMNANTS OF INTESTINAL DIGESTION.

The Fæces.

The fæces represent that part of the contents of the alimentary tract which is not absorbed into the circulation. The contents represent not only the ingested food but portions of various secretions and of excretions, besides bacteria and their excreta, and epithelial elements from the mucous membrane. The bulk of the fæces is modified by the proportion of indigestible material in the ingesta. The fæces of the herbivora are very copious, while those of carnivora are comparatively scanty. In man the weight will vary from 170 gms. to 400–500 gms. according to diet. The amount of water varies with the character of the food and with the habit of the animal; free and frequent passages having more water than those associated with constipation. The longer the fæcal matter is retained the larger the proportion of water absorbed from it.

The composition of the fæces may be classified thus:

Composition of the Fæces.

Gases: N, H, CO_2, H_2S, CH_4.

Liquids: H_2O (68% to 82% normally).

Solids: *Undigested Food.*—Fats, fragments of meat, starch.

Indigestible Matter. Cellulose, ligaments from meat, keratin, mucin, gums.

Bacteria and the resins. *Products* of their Decomposition of Foods. Lower fatty acids, lactic acid, tyrosin and its decomposition products, phenol; hæmatin, insoluble soaps of Ca and Mg.

Bile Residues: Mucus, cholesterin, bilary acids, stercobilin.

Excretin.—$C_{78}H_{156}SO_2$.

Inorganic Salts.—Soluble salts of Na, K, Mg, etc.
Insoluble salts of Ca, Mg, Fe, etc.

5. THE MOVEMENTS OF THE INTESTINES.

The movements of the intestines are together called *peristalsis*. Peristalsis consists of a progressive wave of contraction which usually passes from above downwards. This wave of contraction involves especially the circular fibers whose progressive contraction has the mechanical effect of sliding a small ring along the gut contracting the lumen upon the contents. Accompanying the contraction of the circular fibers and just preceding it is a contraction of the longitudinal fibers. This combined *vermicular peristalsis* is very effective in pushing on the contents of the canal.

The peristalsis of the intestinal tract is stimulated by the presence of food in general; but it is especially stimulated by the presence of such sharp pieces of cellulose as occur in coarse meals of the cereals. The vagus seems to be the efferent nerve. Section of the vagus causes cessation of all reflex peristalsis. Section of the splanchnics causes vaso-dilatation with profuse secretion of the succus entericus.

6. DEFECATION.

Ingestion begins with a voluntary act and is consummated with an involuntary act. Egestion or defecation begins with an involuntary act and is consummated with a voluntary act.

As the food approaches the rectum it gradually loses water and greater force is required to move it along the canal ; accordingly the circular muscular coat is thicker in the lower end of the canal, reaching a maximum in the external sphincter of the anus.

The slow contractions of these muscles gradually advance the fæces to the rectum where their accumulation periodically stimulates a strong expulsatory contraction of the circular muscle fibers of that viscus. This, though purely involuntary, is not outside the consciousness of the individual. The final conscious act consists in voluntarily inhibiting or suspending the tonic contraction of the external sphincter. In the absolutely typical and normal condition the contraction of the walls of the rectum suffices to rid it of the accumulated fæces. Frequently the force of these muscles must be supplemented. This is accomplished by a voluntary contraction of the abdominal muscles, which causes a high pressure within the abdominal cavity, the intravenous pressure in the hæmorrhoidal veins is positive, and there is a tendency for these veins to become permanently distended, causing hæmorrhoids.

CHAPTER VI.

ABSORPTION.

INTRODUCTION.

1. ABSORPTION DEFINED.
2. STRUCTURES INVOLVED IN ABSORPTION.
3. PHYSICAL FORCES INFLUENCING ABSORPTION.
4. FORMER THEORIES OF ABSORPTION, REVIEWED.

THE PHYSIOLOGY OF ABSORPTION.

1. ABSORPTION FROM DIFFERENT PORTIONS OF THE ALIMENTARY CANAL.
   - *a.* Absorption From the Mouth.
   - *b.* Absorption From the Stomach.
   - *c.* Absorption From the Small Intestines.
   - *d.* Absorption From the Large Intestine.
2. ABSORPTION OF DIFFERENT FOODSTUFFS.
   - *a.* The Absorption of Water.
   - *b.* The Absorption of Salts.
   - *c.* The Absorption of Carbohydrates.
   - *d.* The Absorption of Proteids.
   - *e.* The Absorption of Fats.

ABSORPTION. INTRODUCTION.

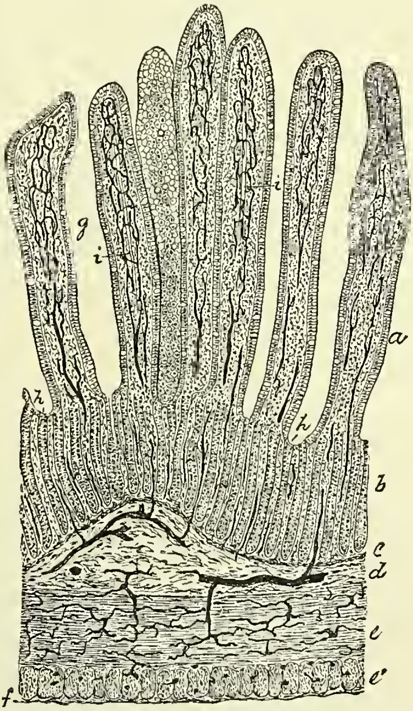
1. ABSORPTION DEFINED.

THE term *absorption* in its general sense means imbibition and applies with special fitness to the *"drinking in"* of a liquid by any porous body such as a sponge. In this sense it is a purely physical process depending upon the *capillary attraction* exerted by the capillary pores of the body upon the liquid. This term has been extended to include such processes as the taking-in of water by germinating seeds, a purely physical process depending upon the laws of diffusion or osmosis. It was the most natural thing to extend the term to the process by which an organism takes up food from the medium in which it exists or from canals in which foods have been dissolved or otherwise prepared. *Absorption,* then, *is that function of the organism, through the exercise of which the system takes in nutriment through a boundary epithelium.* It has been thought that the absorption by the system, of the products of digestion is a purely physical process depending upon the interaction of two or three factors: osmosis, filtration.

Whether or not physical forces alone are sufficient to account for the phenomena of absorption will be discussed later. In the definition of absorption reference was made to the "boundary epithelium." The boundary epithelia of the mammalian body are: (I) the epithelium of the alimentary canal; (II) epithelium of the lung passages; (III) the epithelium of the urinary tract; (IV) the cuticle. Of these boundaries the first is preëminently an absorptive surface while the second is equally absorptive and excretory; the third is wholly excretory, and the fourth is practically non-absorptive; and its excretory and secretory functions are secondary to its especial function—protection.

It will be understood from this expression *boundary epithelium*, that the physiologist looks upon the contents of the alimentary canal, lung passages, and renal passages as being *really outside of the organism though enclosed by the body.* What is in the alimentary canal is really not yet within the organism. When it passes within the outer boundary of the outer layer of cells, then it is within the organism, and the passage from the alimentary canal into the epithelial cells which surround this canal constitutes *absorption.*

Fig. 184.



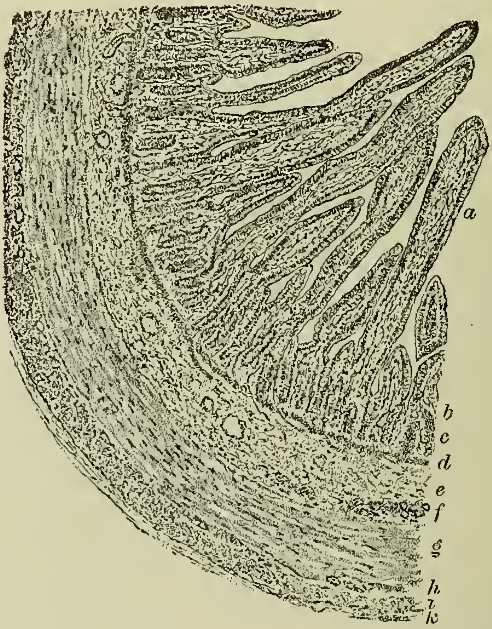
Section of injected small intestine of cat: *a*, *b*, mucosa; *g*, villi; *i*, their absorbent vessels; *h*, simple follicles; *c*, muscularis mucosæ; *d*, submucosa; *e*, *e'*, circular and longitudinal layers of muscle; *f*, fibrous coat. All the dark lines represent blood vessels filled with the injection mass. (PIERSOL.)

2. STRUCTURES INVOLVED IN ABSORPTION.

Whatever forces may be involved in the process of absorption,—whether physical, mechanical, or vital,—the area of absorbing surface must be an important factor in the total amount absorbed.

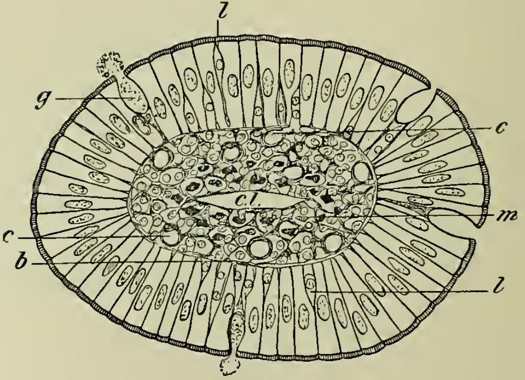
Under *Digestion, Introduction,* mention was made of the prominent transverse folds of the mucosa of the small intestine. These *valvulæ conniventes* make the mucous surface about three times as great as a straight cylindrical lining of the same canal would be. Upon this folded mucous surface the microscope reveals innumerable minute finger-like projections—the villi. These projections are subcylindrical in form and the axis of the cylinder may be

FIG. 185.



Showing the frequent inequality of the villi. (BENDA.)

FIG. 186.

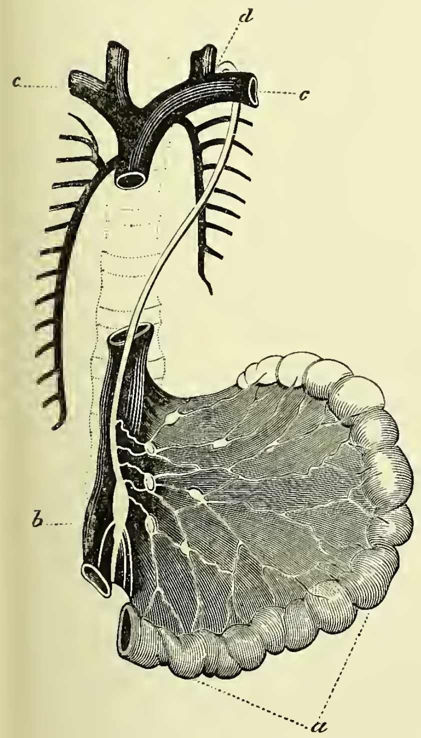


Cross-section of an intestinal villus. *e*, columnar epithelium; *g*, goblet-cell, its mucus is seen partly extruded; *l*, lymph corpuscles between the epithelium-cells; *b*, basement-membrane; *c*, blood-capillaries; *m*, section of plain muscular fibers; *c.l.*, central lacteal. (SCHAEFER.)

taken as averaging about eight times the radius of the base. The area of the villus would then be about 16 times as great as the area of the base, or the area of the whole surface occupied by villi is multiplied approximately 16 times through the means of the villi. Thus the area of the epithelial surface is many times as great as the area of the intestine when considered as a smooth cylinder.

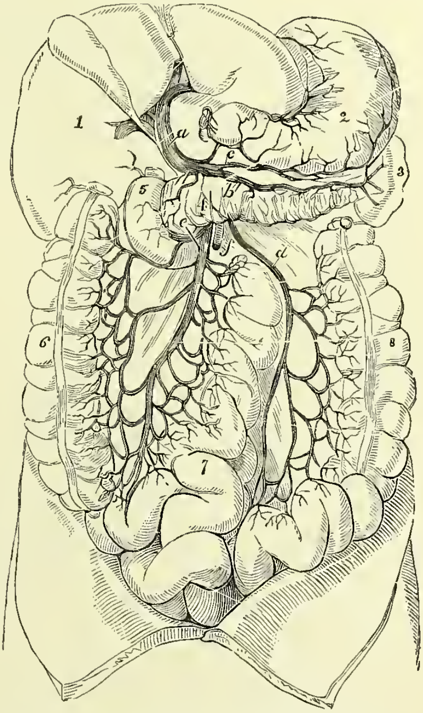
The accompanying figures show the structure and grouping of the villi. Note in Fig. 184 the coats of the intestine: the injected arteries and capillaries; the lymph radical in the second and fifth villi from the left. The ends of the cells shown in the third villus from the left. Fig. 185 shows the marked inequality frequently to be noted in the length of the villi. In Fig. 186 the minute structure of the villus is shown. Note, especially, the numerous capillaries which lie just beneath the basement membrane; the muscle-fibers, and the large "central lacteal" or lymph radicle.

FIG. 187.



Lacteals, thoracic duct, etc. *a*, intestine; *b*, vena cava inferior; *c*, *c*, right and left subclavian veins; *d*, point of opening of thoracic duct into left subclavian. (DALTON.)

FIG. 188.

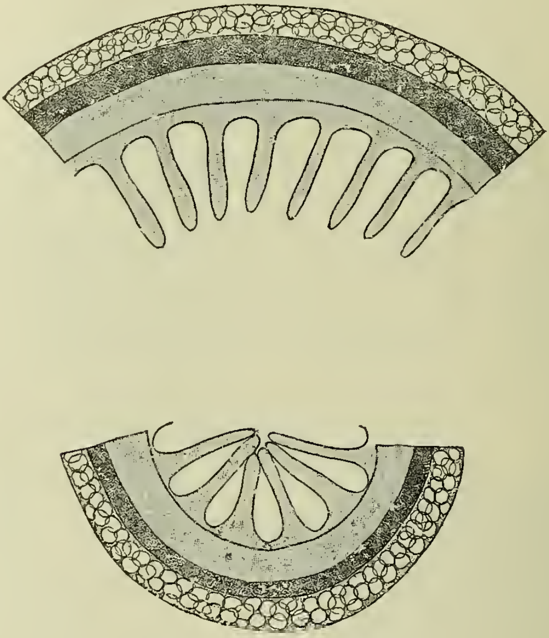


View of the principal branches of the vena portæ. $\frac{1}{6}$. 1, lower surface of the right lobe of the liver; 2, stomach; 3, spleen; 4, pancreas; 5, duodenum; 6, ascending colon; 7, small intestine; 8, descending colon; *a*, vena portæ dividing in the transverse fissure of the liver; *b*, splenic vein; *c*, right gastroepiploic; *d*, inferior mesenteric; *e*, superior mesenteric vein; *f*, superior mesenteric artery. (QUAIN.)

In the intestine of such animals as the cat, rat, and rabbit the longer villi reach well toward the middle of the intestine.

The two courses which absorbed material takes are: (1) through the lacteals, and thoracic duct to the venous system (See Fig. 187); through the vena portæ to the liver (see Fig. 187).

Fig. 189.



Relations of villi during peristalsis.

3. PHYSICAL FORCES INFLUENCING ABSORPTION.

Just how far physical forces enter into the act of absorption has been a subject of controversy for a long time. Recent investigations tend to minimize the importance of the physical forces and to magnify that of the more distinctly physiological factor "selection." The student is, however, unable to understand the literature of the subject without at least a general knowledge of *Osmosis* and *Filtration.*

a. **Osmosis.**

The term osmosis is applied to diffusion taking place through a membrane. But diffusion involves a mutual or reciprocal interchange of space or a mutual interpenetration independent of any mechanical mixture or chemical reaction.

Let the open end of a large glass tube have an animal membrane stretched across it and fixed in place; let the tube be partly filled with a solution of any crystalline substance easily soluble in water; and let this dialyzer or endosmometer be lowered into a jar or beaker of distilled water until the liquid within the dialyzer stands on the same level as that outside. These conditions fulfilled, one will observe, after a few hours, that the liquid within is higher than that in the beaker outside, making it evident that water has passed through membrane into the dialyzer or osmometer. A chemical test of the liquid outside readily reveals the fact that some of dissolved salt has passed through the membrane into the distilled water. The raising of the liquid in the dialyzer above the level of that outside involves a certain amount of energy. This energy is measurable and may be determined with a mercury manometer or by simply calculating the weight of the column of water supported by the pressure. This is called *endosmotic pressure* or *osmotic pressure.*

1. **Laws of Osmotic Pressure.**—The work done by Pfeffer ("Osmotische Untersuchungen," Leipzig, 1877) establishes the following laws of osmotic pressure:

Law I. "*The osmotic pressure of a dilute solution at constant temperature is proportional to its concentration.*" (Reid, in Schaefer's Text Book, Vol. I., p. 265.)

Law II. "*At constant concentration of a dilute solution the osmotic pressure is proportional to the absolute temperature.* (Reid.)[1]

These two laws are well illustrated in the following data from Pfeffer's "*Untersuchungen.*" *Cane sugar was used.*

I. Varying Concentration; Constant Temperature (14° C.)

II. Varying Temperature, Constant Concentration (1 Per Cent.).

Concentration of Solution.	Osmotic Pressure in mm. of Hg.	Temperature.	Pressure.	
			Observed.	Calculated.
I. 1 %	535	II.		
2 %	1016	32°	544	
4 %	2082	14.15°	510	512
6 %	3075	36°	567	
		15.5°	520	529

Note that law I for osmotic pressure is the equivalent of Boyle's law for the *pressure volume* of a gas; and that law II is the equivalent of Charles' law for the temperature-volume of a gas.[2]

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[1] *The absolute temperature* (in degrees centigrade) is calculated from — 273° C. as an *absolute zero.* Thus a temperature of 15° C. equals (273 + 15) 288° Abs.

[2] *Charles' Law*: "The volume of a gas, if the pressure remain the same, is directly proportional to its absolute temperature. If the pressure and volume both vary, then their product is proportional to the absolute temperature." (Daniell's Physics, p. 77.)

LAW III: "*The osmotic pressure of a dissolved substance is exactly the same as the gas pressure, measured by the manometer, which one would observe if he could remove the solvent and leave the dissolved substance as a gas filling the same volume.*" (Nernst's "Theoretical Chemistry." Cited by Reid.)

Van't Hoff calls attention to the fact that "the hypothesis of Avogadro[1] then is not merely capable of extension by the law of Henry to solutions of gases, but to solutions of matter which is not gaseous under ordinary circumstances. From the foregoing Reid formulates the following:

LAW IV: "*Equal volumes of gases or dilute solutions at the same gas or osmotic pressure, and at the same temperature, contain equal numbers of molecules.*" (Schaefer's Text-book of Physiology, Vol. II., p. 266.)

Within certain limitations Dalton's law for gas mixtures[2] holds for the osmotic pressure of a mixture of substances:

LAW V. "*The total osmotic pressure of a mixture of substances* (in solution) *is equal to the sum of the partial osmotic pressures of the several components.*" (Reid.)

Adie (*Jour. Chem. Soc. London*, 1891, Vol. LIX., p. 344, cited by Reid) calls attention to the fact that "when the two or more constituents of the solution have a common *ion* each salt *diminishes* the dissociation of the other, so that the pressure of the mixture is less than the sum of the pressures of the two components.

For example the osmotic pressure of 1:40 solution of $Al_2(SO_4)_3$ is 1.27, of a 1:40 solution K_2SO_4 is 1.29. The sum of the pressures is thus 2.56. But the pressure of 1:40 solution $K_2Al_2(SO_4)_4$ is not 2.56 but 2.39.

The osmotic pressure of a solution is a measure of the osmotic activity. The above laws take into consideration only *temperature*, *degree of concentration*, and the *influence* of mixtures; but most important factors are the *character of the membrane* and of the *solvent*.

Summing up this brief discussion of osmosis one may give the following factors as concerned in the rate of osmosis:

(I) The quantitative composition of the solutions separated by the membrane, and consequently the partial osmotic pressure exerted by the several constituents.

(II) The coefficients of diffusion of the various constituents.

(III) The character of the membrane.

(IV) The character of the solvent.

(V) The temperature.

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[1] Avogadro's hypothesis: *Equal volumes of all gases contain the same number of molecules.*

[2] The pressure exerted by each component of a mixture of gases is independent of the pressures exerted by the rest of the components.

(VI) The hydrostatic pressure upon the two sides of the membrane (filtration).

b. Filtration.

Filtration is the passage of a liquid through a membrane under the influence of pressure. It is a purely mechanical process. In the animal body any filtration which may occur is complicated with an osmosis which is going on at the same time, for in every case the relation of liquid, membrane and filtrate are such as have just been described under osmosis.

In fact factor (VI) above gives *hydrostatic pressure* as one of the variables, so that in the living organism cases of filtration may be classified as cases of osmosis where the principal determining factor is *hydrostatic pressure.*

The following factors are active in filtration :

(I) The porosity of the membrane.
(II) The degree of pressure.
(III) The character of the liquid to be filtered.
(IV) The temperature of the liquid.
(V) The action of the liquid upon the membrane.
(VI) The osmotic relations of liquid to filtrate.

4. FORMER THEORIES OF ABSORPTION REVIEWED.

a. The Vital Energy Theory.

The earlier theories of the physiologists regarding the forces involved in absorption are very well represented by Tiedemann and Gmelin (quoted by Heidenhain, *Arch. f. d. ges. Physiol.*, 1888, Bd. XLIII., S. 69) who likened it to *secretion*, and conceived that it was practically the same process *reversed* in *direction ;* he ascribed to the cell the force necessary to accomplish this work and looked upon it as one of the manifestations of the vital energy of the cell.

b. The Physical Theory.

The next generation of physiologists experienced a reaction against the vital-energy theory. The physical phenomena of diffusion, osmosis, and imbibition were better understood. Ludwig, Brücke and their associates were devoting their energies toward the solution of physiological problems through the laws of chemistry, physics and mechanics. These efforts had a most salutary effect upon physiology. That field of human knowledge assumed under these men the dignity of an experimental science. The methods of investigation were the exact methods of the chemical or physical laboratory.

It was the hope of this school of physiologists to account for all of the phenomena of life as the manifestation of the action, and more or less complex interaction of the forces already known in chemistry and physics. They considered that the processes of digestion are chemical processes, pure and simple; that *the processes of absorption are physical and mechanical processes pure and simple.*

The epithelium of the alimentary canal represents a dialyzer membrane: on one side is the blood containing non-diffusible proteids, on the other the products of digestion containing diffusible proteids. If the salts in the contents of the alimentary canal make too strong a solution (*e. g.*, $MgSO_4$) water diffuses rapidly into the canal and a serous catharsis follows. In the usual relation between the blood plasma and the contents of the canal the water readily diffuses into the blood. Filtration was invoked to assist osmosis where that failed to satisfy the requirements. Brücke called attention to the fact that peristalsis causes an increased pressure in certain portions of the canal. The contraction of the villi empties them, driving the contents of the lymph radical on into the lacteals, and the contents of the capillaries on into the venules of the portal system. The valves in the lacteals and the veins prevent regurgitation of the lymph and blood when the muscles of the villi relax. The natural elasticity of the villi tends to cause them to regain their original size thus making a negative pressure within the villi. Attention was also called to the fact that at the point where a peristaltic wave contracts the canal to one half or one third its usual lumen the *apices* of the villi come together while there is still liquid around their bases (Fig. 188). A further contraction puts the liquid thus enclosed under pressure. The direction of this pressure will assist its filtration into the villi.

Absorption of fat globules was looked upon as a purely mechanical process in which the epithelial cells through their marginal rods or the lymph corpuscles engulfed the globules and transported them bodily to the lacteals. It was expected that this array of physical and mechanical forces would account for all the phenomena of absorption. More searching investigations on the part of the champions of the physical theory revealed the inadequacy of physical laws, as understood by physicists to account for the observed physiological phenomena.

c. **The Selection Theory.**

The pendulum of thought has swung back toward the vital theory again. We do not use "vital energy" in our terminology because the literature of the past prejudices us against that expression. We say knowingly that the cell "*selects*" the materials which are to be absorbed, but the mystery is as great in *selection* as when the thing was accomplished by virtue of a "vital energy." Moore sums up well our present views on absorption. "The cells of a secreting gland take up certain materials from the lymph in which they are bathed, and from these, in some manner, elaborate certain products which are passed into the gland lumen as a secretion. Similarly, the absorbing cells of the intestine take up certain products of digestion from the intestinal contents by which they are bathed, and build up from these, certain materials which pass into the lymph (and plasma). *So that absorption may be regarded as a sort of reversed secretion. In both cases the process is a selective one.*

The character and rate of the *secretion* are much influenced by the amount and the pressure of the blood in the gland; similarly the character and rate of absorption are influenced by the conditions which exist in the alimentary tract. Instead of looking upon the physical forces of diffusion and pressure as the *sole* factors of absorption we now recognize them as *modifying* factors.

The following are some of the facts which prove that the process of absorption is not one of simple diffusion: (*a*) Alkali-albumin and acid-albumin are practically indiffusible, yet they are readily absorbed from the large intestine, also from a loop of small intestine in the absence of all proteolytic enzymes. (*b*) "The rate of absorption, from the intestine, of various dissolved substances is not proportional to their diffusion coefficients." Röhmann (*Arch. f. d. ges. Physiologie*, Bd. XLI., S. 411), found that from a mixture of equal parts of Na_2SO_4 and dextrose the more slowly diffusible dextrose is much more rapidly absorbed than the sodium salt. *These facts and many others lead physiologists to attribute to the selective power of the living epithelial cells the typical phenomena of absorption, recognizing meantime that osmosis and filtration are modifying factors.*

THE PHYSIOLOGY OF ABSORPTION.

1. ABSORPTION FROM DIFFERENT PORTIONS OF THE ALIMENTARY CANAL.

a. Absorption from the Mouth.

That a certain amount of the soluble portions of the food is absorbed by the mucous membrane cannot be doubted. But oral absorption is solely incident to the sense of taste and is too slight to be taken into account as a factor in nutrition.

b. Absorption from the Stomach.

The investigations of recent years tend to minimize the importance of the stomach, not only in digestion, but also in absorption. Before the subject was investigated with sufficient care it was taught that water and salts are absorbed freely by the stomach. It may be demonstrated, however, that only a very small proportion (about 1 per cent.) of the water is absorbed even when a considerable quantity of water alone is taken into the stomach.

Salts and sugars in solution are absorbed most readily when the degree of concentration is considerable; the minimum degree at which absorption may take place being 3 per cent. for salts and 5 per cent. for sugars; the most favorable degree of concentration being 20 per cent. for grape sugar while in the small intestine it is 0.5 per cent.

The proteoses and peptones are probably absorbed to a certain extent by the gastric mucous membrane, at any rate the presence of these products of gastric digestion greatly stimulates the activity of the gastric glands.

Alcohol is freely and rapidly absorbed by the stomach.

c. Absorption from the Small Intestines.

Absorption from mouth and stomach seems to be purely incidental. If there is a specialized organ of absorption, that organ must be the villus of the small intestine. The villus seems to be especially fitted structurally for absorption; it is the organ which absorbs nearly all of the liquid nutriment for the organism; no other function may be ascribed to it.

These considerations justify us in calling *the villus the organ of absorption.*

From the lumen of the small intestine the villi absorb the products of gastric and of intestinal digestion; sugars, proteoses, peptones, fatty acids, soaps, water, salts, etc.

d. Absorption from the Large Intestine.

Water and salts are readily absorbed by the large intestine. This viscus seems to be an important site for the absorption of water, as the intestinal contents pass the ileocæcal valve in a liquid state—simulating chyme—and enter the rectum in a pasty condition, the water having been largely absorbed.

About 14 per cent. of the proteids and small amount of sugars and fats are also absorbed from the large intestine.

Most interesting of all is the fact that enemata of undigested proteid, syntonin or alkali-albumin, even dilute egg-albumin, is absorbed in sufficient quantity to nourish an animal.

2. THE ABSORPTION OF DIFFERENT FOODSTUFFS.

a. The Absorption of Water.

As has been stated above water is absorbed principally from the small and large intestines. The portion absorbed from the former is absorbed mostly from the lower segment, namely the ileum, while it is the first portion of the large intestine that takes up most of the water which remains in the intestinal contents when they pass the ileocæcal valve.

The significance of these facts regarding the absorption of water is not difficult to see. If the water were largely absorbed in the stomach and the upper part of the small intestine the absorption of the other products of digestion from the small intestine would be much hindered, because experiment has shown that the absorption of the dissolved foodstuffs is much facilitated by dilute solutions. Furthermore the movements of a viscous mass, deprived of most of its water, would be much hindered.

Altogether it seems most natural and advantageous for the water to be absorbed late in the general process of absorption.

b. The Absorption of Salts.

If the laws of diffusion dominate the process of absorption, and if osmotic pressure is the principal force involved in this process, we shall expect to see these physical laws and forces especially evident in the absorption of salts and their solvent water. The serous catharsis referred to above seems to be an example of a diffusion of water from the blood into the lumen of the intestine, induced by the high concentration of the salt solution in the intestine. When such conditions exist in a dialyzer, water passes through the membrane from the less concentrated into the more concentrated solution, while salt passes from the more concentrated into the less concentrated solution. The watery stools following ingestion of strong solutions of $MgSO_4$ and related salts seem to confirm this theory. Recent experiments by Wallace and Cushny ("Intestinal Absorption and Saline Cathartics," *Am. Jour. Physiol.*, Vol. I., No. IV., July, 1898) show that "Dilute solutions (isotonic) of the saline cathartics retard the absorption of fluid from the stomach and small intestine, and thus act by rendering (keeping) the contents more watery and more easily moved through the lower parts of the alimentary canal." * * * "They (dilute solutions of the cathartics) do not necessarily increase the fluid of the bowel, but merely fail to be absorbed and thus render the fæces more fluid and more easily moved through the large intestine."

The same observers found that if a hyperistonic solution of $MgSO_4$ be introduced into the intestine it is reduced to the isotonic condition by interchange with the blood; while if a hypistonic solution of $MgSO_4$ be introduced into the intestine it is raised to the isotonic condition by interchange with the blood, probably by giving up water to the blood.

If instead of using one of the salts, which clinical observations have led us to classify as cathartic salts, NaCl be used it will be found (Heidenhain, *Pflüger's Archiv.*, 1894, Vol. 56, S. 579) that dilute solutions (0.3–0.5 %) are completely absorbed, both the water and the salt passing into the blood. Wallace and Cushny observed a similar phenomenon.

Evidently, then, the absorption of salts (and water) obeys the laws of diffusion more or less faithfully *according to the salt in solution.*

Why NaCl should pass the epithelial boundary so readily while the passage of $MgSO_4$ is practically barred out, can only be accounted for on the basis of a selective act on the part of the epithelial cells. From the accounts of experiments with the two classes of salts represented by NaCl and $MgSO_4$ one can scarcely avoid the conviction that the presence of such salts as $MgSO_4$ in the intestine affects the epithelium *by suspending its selective power and reducing them to a mere passive membrane subject to the laws of simple diffusion.* That such an effect, especially when produced by strongly hyperistonic solutions may be deleterious to the system is not unlikely. The question deserves investigation.

Summarizing, one may say: *The soluble salts, common in the foods, are readily absorbed by the epithelium of the small intestine. The absorption, though influenced by the laws of diffusion, responds primarily to the selective power of the epithelial cells.*

c. The Absorption of Carbohydrates.

The whole process of carbohydrate digestion points toward the monosaccharids as the form in which carbohydrates are to be absorbed.

The fact that only the monosaccharids, especially dextrose, may be found in the blood of the portal vein seems to confirm this indication. Rohmann (*Pflüger's Arch.*, 1887, Bd. XLI., S. 411) found that starch solution disappears rapidly from an intestinal loop. The succus entericus has almost no action upon starch. It must then be absorbed as starch by the epithelial cells. It leaves those cells as dextrose. The cells must, then, have the power to digest starch. Experiments of other investigators also point to similar conclusions.

Under the usual conditions, however, it is certain that by far the greater part of the carbohydrates is absorbed in the form of monosaccharids, *dextrose, levulose, galactose,* from the small intestine, an unimportant fraction may be absorbed in the form of disaccharids, or even polysaccharids; a small proportion is absorbed by the stomach and large intestine.

d. **The Absorption of Proteids.**

As in the case of carbohydrates so in the case of proteids the processes of digestion are processes of solution and change from indiffusible to diffusible forms. That the solution of proteids is necessary would seem certain; yet, diluted, not dissolved, egg-albumin is absorbed from the large intestine when given as an enema; and diluted egg-albumin is absorbed (16–33 per cent.) from a loop of intestine in the absence of all proteolytic enzymes. Actual chemical solution is then not a necessary preliminary to absorption; it is only necessary that the proteid be in a dilute liquid form. When the ideas of physiologists on this problem were made to harmonize with the osmosis theory the reduction to a *diffusible* peptone was looked upon as a necessary preliminary to absorption. Though peptone is diffusible its diffusibility is much too low, its rate much too slow, to account for what actually takes place in the alimentary canal. Acid-albumin or alkali-albumin is absorbed from a loop of intestine almost as completely as are peptones and proteoses, though much more slowly than they (*i. e.*, about 60–70 per cent. in 24 hours.—Huber, 1891). The amount of *leucin, tyrosin,* and allied bodies formed in normal digestion is probably very small because of the rapid absorption of the proteoses and peptones; naturally then the amount of these amido-acids normally absorbed will be small. A small amount of proteids is absorbed from the stomach, about 14 per cent. from the large intestine, and all the remainder—80–85 per cent.—from the small intestine.

Summary: *A large proportion of the proteids are absorbed by the small intestine in the form of proteoses and peptones. A small part of the proteids may be absorbed from the alimentary canal in the form of alkali-albumin or acid-albumin or even as native proteid.*

e. The Absorption of Fats.

The digestive processes of the small intestine change fat to a mixture of: fatty acids, glycerine, soaps, and emulsified fats. The fatty acids are soluble in the bile acids. Glycerine and the sodium and the potassium soaps are soluble in water, calcium and magnesium soaps are soluble in the bile salts,—probably changed to sodium soaps. The large amount of emulsion as compared to the amounts of the other forms found in the intestine together with the discovery of innumerable oil globules in the epithelial cells during absorption; and the appearance of oil globules,—emulsion, in the chyle of the lacteals during absorption led physiologists to conclude that the fat is absorbed, for the most part, in the form of an emulsion. Earnest efforts have been made to reconcile this theory with the recognized limitations of fixed epithelial cells.

Before we accept the emulsion theory of absorption the following facts should be considered:

(*α*) Ingested soluble soaps are absorbed (Radziejewski, *Virch. Arch.*, Bd. LVI., S. 211—cited by Moore).

(*β*) Soap and glycerine are absorbed and synthesized, after absorption and before the lacteals are reached, into neutral fat which circulates through the lacteals as a typical chyle emulsion. *The epithelial cells when treated with osmic acid show abundant oil globules.* (Perewoznikoff, cited by Moore, *Schaefer's Physiology*, Vol. I., p. 451.)

(*γ*) Ingestion of free fatty acid and glycerine is followed by a synthesis within the epithelium and the appearance of fat globules there. (Will., *Arch. f. d. ges. Physiol.*, Bd. XX., S. 255, quoted by Moore.)

(*δ*) Ingestion of free fatty acid *alone* was followed by the appearance of fat globules in the epithelial cells. In this case the cells must have furnished, from some source, the glycerine constituent of the fat formed.

(*ε*) Steapsin acts rapidly upon the fat and in the usual time consumed in intestinal digestion would be able to change the usual amount of fatty food into fatty acid and glycerine. (Rachford, in *Jour. Physiol.*, Vol. XII., p. 92, quoted by Moore.)

(*ζ*) It has been objected to the soap theory that the amount of Na_2CO_3 necessary to saponify the fat of one meal would be three or four times as much as the whole body contains. Moore calls attention to the fact that once the soap passes into the epithelium the Na is of no further use in the cell and can be used over and over again as a carrier. One can conceive of a sodium atom (I) being carried into the intestine as a part of the secretion combined with CO_2; (II) dropping the CO_2 to join with a molecule of palmitic or other fatty acid and passing into the cell; (III) dropping the palmitic acid for —OH; (IV) passing to the intestinal surface of the cell; (V) saponifying another molecule of palmitic acid carrying it into the cell; and again joining with —OH, etc., etc., repeating the cycle indefinitely. The formation of soap on the outer side of the epithelium is a spontaneous chemical reaction. The breaking up of that molecule to liberate palmitic acid for synthesis with glycerine and Na for synthesis with —OH is probably due to a ferment action of the cell. Note that a mystic vital force is called in at the critical point. The same force must be invoked to put the NaOH out on the proper side of the cell.

(γ) Fatty acids are soluble in bile acids. A series of observations by Altmann and by his pupil, Krehl (*Arch. f. Anat. u. Phys.*, Leipzig, 1889, Supl. Bd., S. 86, cited by Moore) show that the fatty acids dissolved in the bile acids are absorbed, and synthesized into neutral fats with formation of fat globules in the epithelium.

From the observations above cited it is evident: (I) That the appearance of fat globules in the epithelial cells and the lacteals does not necessarily demonstrate that the fat is absorbed as an emulsion; (II) that the appearance of fat globules in the epithelial cells and the lacteals after ingestion of soaps or of fatty acid and glycerine does demonstrate that the elements of fats may be absorbed in this form and neutral fat synthesized by the cells from the elements; (III) that special cell activity is necessary in either case.

When two alternatives are presented the physiologist is wise to accept with suspended final judgment the one which is most reasonable and most in harmony with other similar processes. Absorption of fat in globules is wholly inexplicable; absorption of fat in solution, as soaps and fatty acids, is only partly inexplicable.

Summary: THE EMULSION THEORY *of fat absorption is that by far the greater part of the fat passes into the cells in the form of small globules, neutral fat in emulsion, or of fatty acid in emulsion, while a minute portion may be absorbed as soap.*

THE SOLUTION THEORY *of fat absorption is that at the moment of entering the epithelial cell the fat or fat elements are in solution either as soaps in aqueous solution or as fatty acids in solution in bilary acids; that the absorbed elements are synthesized in the epithelial cell forming neutral fat which appears in globules, and that these globules pass from the cells into the lacteals, forming the milky chyle.*

CHAPTER VII.

METABOLISM.

INTRODUCTION.

1. METABOLISM DEFINED AND CLASSIFIED.
2. METABOLIC TISSUES AND ORGANS.
3. THE INCOME AND OUTGO OF MATTER.
4. EQUILIBRIUM.
5. THE CIRCULATION OF THE ELEMENTS.
6. THE CIRCULATION OF TYPICAL COMPOUNDS.
7. THE CHARACTER OF THE METABOLIC CHANGES.

ANIMAL METABOLISM.

A. METABOLIC CHANGES OF DIFFERENT CLASSES OF FOODSTUFFS.

1. CARBOHYDRATES.
    - *a.* Absorption Form.
    - *b.* Circulation Form.
    - *c.* Metabolism.
    - *d.* Excretion of Carbohydrate Katabolites.
2. PROTEIDS.
    - *a.* Absorption Form.
    - *b.* Circulation Form.
    - *c.* Metabolism.
    - *d.* Nutritive Value of Proteids.
    - *e.* Laws of Nitrogen Equilibrium.
3. FATS.
    - *a.* Absorption Form.
    - *b.* Circulation Form.
    - *c.* Metabolism.
    - *d.* Fat Deposit.
4. THE INTER-RELATIONS OF THE FOODSTUFFS IN NUTRITION.

B. SUMMARY OF ANABOLISM AND KATABOLISM.

1. ANABOLISM.
2. KATABOLISM.

C. THE INCOME OF ENERGY.

1. THE POTENTIAL ENERGY REPRESENTED BY THE FOODSTUFFS.
2. THE POTENTIAL ENERGY REPRESENTED BY COMMON FOODS.
3. THE ENERGY REPRESENTED BY A TYPICAL MENU.

D. THE LIBERATION OF ENERGY.

1. THE LIBERATION OF THE POTENTIAL ENERGY OF THE ORGANISM.

2. THE TRANSFORMATION OF ENERGY.
3. THE CONSERVATION OF ENERGY.
4. THE EXPENDITURE OF THE KINETIC ENERGY OF THE ORGANISM.

E. ANIMAL HEAT.

1. GENERAL CONSIDERATIONS.
2. METHOD OF DETERMINING THE MEAN TEMPERATURE.
3. FACTORS WHICH CAUSE VARIATIONS OF THE TEMPERATURE.
   (1) CLIMATE. (2) SEX. (3) AGE. (4) SEASONS. (5) EXTREME TEMPERATURE ARTIFICIALLY PRODUCED. (6) DAY AND NIGHT. (7) MUSCULAR WORK. (8) MENTAL WORK. (9) FOOD. (10) SLEEP. (11) BATHS. (12) DRUGS. (13) INDIVIDUAL DIFFERENCE. (14) LIMITS OF TEMPERATURE COMPATIBLE WITH LIFE.
4. TEMPERATURE TOPOGRAPHY IN MAN.
5. HEAT REGULATION OR THERMOTAXIS.

METABOLISM.

INTRODUCTION.

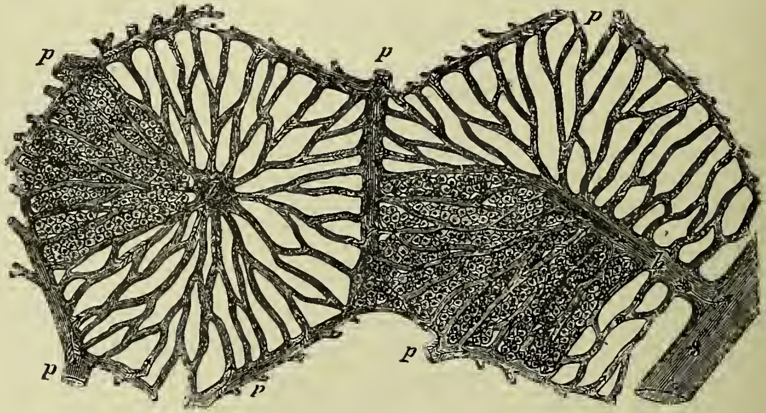
1. METABOLISM DEFINED AND CLASSIFIED.

THE German physiologists were first to separate out from the general territory of nutrition a separate field in which to include all those chemical processes by which matter is transformed from non-living nutrients to living protoplasm, and from living protoplasm to dead excreta. This *change* of *matter* was called *Stoffwechsel*; our technical term METABOLISM is used to cover the same field. Reference was made to the building up of nutrients into living protoplasm and a reversed process. These two phases of metabolism are called respectively *Anabolism* and *Katabolism*. These terms are not so circumscribed, however, as might seem from the foregoing: *Anabolism* includes all those chemical changes by which molecular structure becomes more complex and *energy is made latent*; while katabolism includes all the chemical changes by which molecular structure becomes more simple and *energy is liberated*.

2. METABOLIC TISSUES AND ORGANS.

All specialized functions of the living organism are performed by specialized tissues or organs or systems of organs. Metabolism is not a specialized function; it includes the chemical phases of all tissue activity, and is usually incidental to a primary function. For example: the primary function of the glandular tissues is secretion; but incidental to the secretion is a series of chemical changes which may be considered under the head of metabolism. In a similar manner muscular and nervous tissue possess primary functions peculiar to them and undergo metabolic changes in the performance of those functions. All active tissues, then, are metabolic tissues. The metabolic tissues may be classified as: *muscular*, *nervous*, and *glandular*. If there is an organ that may properly

Fig. 190.



Diagrammatic representation of two hepatic lobules. The left-hand lobule is represented with the intralobular vein cut across; in the right-hand one the section takes the course of the intralobular vein. *p*, intralobular branches of the portal vein; *h*, intralobular branches of the hepatic veins; *s*, sublobular vein; *c*, capillaries of the lobules. The arrows indicate the direction of the course of the blood. The liver-cells are only represented in one part of each lobule. (Schaefer.)

Fig. 191.

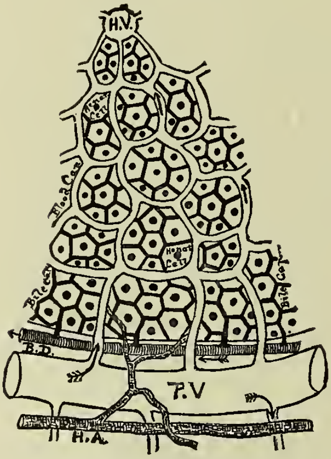
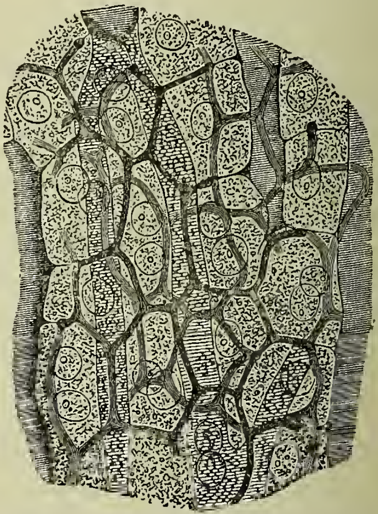


Diagram of the structure of the liver. *P. V.*, the portal or interlobular vein, which breaks up into the capillary network of the lobule; *H. V.*, central intralobular vein, a branch of the hepatic; *H. A.*, hepatic artery, supplying nutrition to the interlobular structures and terminating in the lobular capillary network; *B. D.*, the interlobular bile-duct which takes up the bile-capillaries at the periphery of the lobule. (Piersol.)

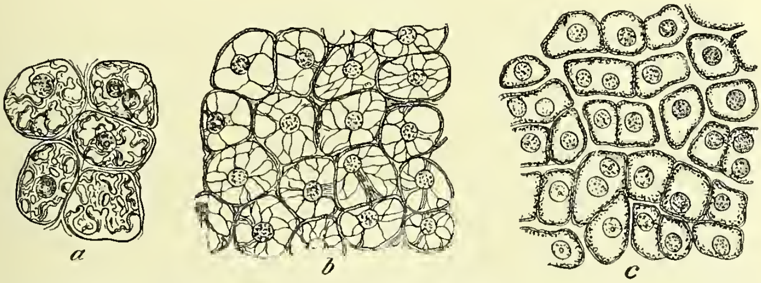
Fig. 192.



Section of rabbit's liver with the intercellular net-work of bile-canaliculi injected. (Highly magnified.) Two or three layers of cells are represented; *b*, blood-capillaries. (From Schaefer after Hering.)

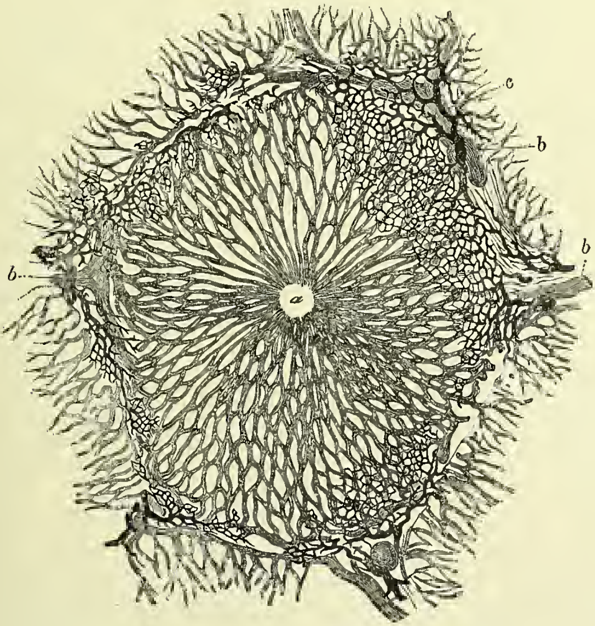
be classified as an organ of metabolism, that organ is the liver. The *external* secretion of the liver is made up largely of substances which are practically useless to the system. The *internal* secretion is composed either of substances on their way to excretion or to further katabolism in the muscles. To be concrete, the bile pigments, salts, and acids, the urea and uric acid, and the glycogen and dextrose are products of liver metabolism. Metabolism is its principal function. The liver is the great central

FIG. 193.



Hepatic-cells still containing glycogen, *a*, and with their glycogen dissolved out, *b*, *c*. In *c* there was less glycogen present than in *b*, and the section is differently prepared. (From SCHAEFER after HEIDENHAIN.)

FIG. 194.



Lobule of rabbit's liver, vessels and bile-ducts injected. *a*, central vein; *b*, *b*, peripheral or interlobular veins; *c*, interlobular bile-duct. (CADIAT.)

whirlpool of the circulating nutrients; it is the center of body metabolism; it may be called the *organ of metabolism.* The anatomical features of the liver which are of special importance to the physiologist may be thus summarized:

1. The liver is supplied with blood from two sources: (*a*) Portal venous system from the capillaries of the intestines to the interlobular branches of the portal veins. (*b*) Hepatic artery bringing arterial blood which mixes with the portal blood within the lobule. (See Figs. 190 and 191.)

2. The hepatic veins collect the blood and carry it to the vena cava. (See Fig. 191.)

3. The bilary secretion is collected by minute bile capillaries, the mesh-work of which is so fine that every secreting cell is in contact with a bile capillary on at least two sides. (See Figs. 192–193.)

4. The bile secretion is collected at the periphery of the lobule by the interlobular bile ducts. (See Fig. 194.)

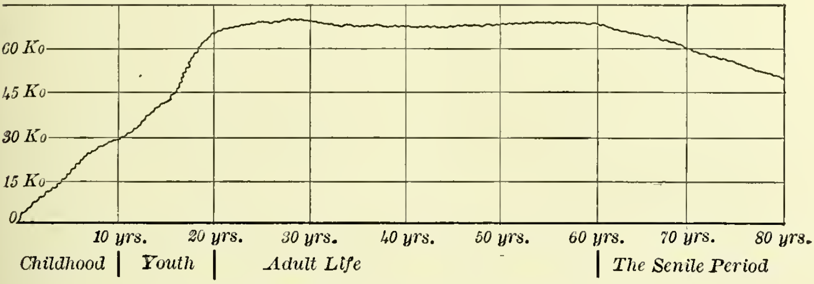
3. THE INCOME AND OUTGO OF MATTER.

The manifestations of life are the manifestations of kinetic energy. In the animal organism the energy is received as potential chemical energy and expended almost wholly as kinetic energy. As far as it is known, energy exists in nature only in association with matter: gravitation, molor motion, chemism, heat and light are all intimately associated with matter, and if transmitted, that transmission can take place only through the agency of matter. If, then, the animal organism is to receive, transform and expend energy, it must receive, transform and excrete matter. The whole process is called nutrition. We have followed the process through the reception of food materials into the alimentary canal, their partial transformation (their digestion) in the stomach and intestine and their absorption into the organism. The amount of the income is the amount of absorbed matter, and the amount of the outgo is the sum of the excretions from kidneys, skin, lungs, etc.

4. EQUILIBRIUM.

If the absorbed matter equals in weight the excreted matter, the body will neither increase nor decrease in weight; it will be in *equilibrium.* Perfect equilibrium seldom exists; during youth there is a gradual increase in weight; during adult life there is approximate equilibrium, while during the senile period there is usually a gradual decrease in the body weight. But this only indicates the general course of the curve of income and outgo. Many factors enter into the problem of body growth and equilibrium to cause numerous minor curves to be superimposed upon the general curve. The occurrence of one or two large waves on that part of the curve which represents the period of growth gives rise to the "*wave-theory of growth.*" Besides these large waves there are small waves occurring each year, and possibly even smaller diurnal waves, so that the composite curve would be something like the following :

Fig. 195.



Curve showing the variation of weight with advancing age.

The *Physiological test* of equilibrium is made by taking the weight at short intervals. The method is like getting an idea of business by noting the daily balances, it shows the equilibrium but gives only a vague idea of the magnitude of the exchange between debits and credits. In the *chemical* test of equilibrium, on the other hand, the debits and credits of an organism are determined by finding the quantity of absorbed material and by determining the quantity of urea, water and carbon dioxide excreted. If the nitrogen of the egesta equals the nitrogen of the ingesta, the organism is said to be in a state of "nitrogen-equilibrium." If the total egesta equals the total ingesta the organism as a whole is in a state of equilibrium.

5. THE CIRCULATION OF THE ELEMENTS.

(*a*) Carbon.—This element enters the system as an important constituent of all the foodstuffs. It is built up into all of the tissues and eventually it is combined with oxygen to form CO_2, which is excreted by the lungs in the gaseous form, or it may be combined with O, N, and H in urea or uric acid, etc., and excreted by the kidneys.

(*b*) Hydrogen enters the system as a constituent of all foodstuffs including water. Like carbon it is a constituent of all tissues. It is excreted in the form of H_2O by kidneys, skin, and lungs ; though a part is excreted as a constituent of urea, uric acid and allied bodies. Most of that hydrogen which enters the system combined with oxygen in water leaves the body as water, never having been separated from the oxygen.

(*c*) NITROGEN is brought to the system only through the proteid foods. It is a necessary constituent of all active tissues, muscle-tissue, glandular-tissue, and nerve-tissue. In the metabolism of the tissues it is, step by step, freed from its complex combinations until finally it is excreted by the kidneys with C, H, and O in urea, uric acid, etc.

(*d*) OXYGEN enters the system uncombined and variously combined. As a gas it enters the lungs, is taken up by the hæmoglobin, transported to the tissues where it plays a prominent part in katabolism. It finally leaves the cell combined with H in H_2O, with C in CO_2, or with C, H and N in urea or uric acid. In these forms it is excreted by the lungs, skin or kidneys. A large quantity of oxygen enters the system in combination in the various foodstuffs. This part of the oxygen is excreted in the same combinations as the oxygen of respiration.

(*e*) PHOSPHORUS enters the system with the proteids. Though phosphorus is a constituent of few proteid foods (nuclein, nerve-tissue, blood-plasma, lymph, and milk), one or more of these is usually associated with each kind of nitrogenous food, so that the system receives a considerable amount. In the body it is a constituent of the tissues and fluids enumerated above; and, combined as $Ca_3(PO_4)_2$, it is a most important constituent of bone. It is excreted by the kidneys as calcium, magnesium or ammonio-magnesium phosphate.

(*f*) SULPHUR is received in combination in proteids, is built up into the body-proteids and is excreted by the kidneys as free sulphuric acid, or as $HKSO_4$ or $HNaSO_4$, or it may be joined to phenol as phenolsulphuric acid, phenolsulphate of potassium, etc.

(*g*) CHLORINE enters the body in combination with sodium. As far as is known, it is separated from this combination, if at all, only in the parietal cells of the peptic glands. That part of the HCl which is absorbed from the alimentary canal comes into contact with Na_2CO_3, or $NaHCO_3$ of the blood and forms H_2O, CO_2 and NaCl, which are excreted.

(*h*) IRON is the most important of the metals and at the same time is the most difficult one of them to absorb and assimilate. Recent investigations of Bunge and others demonstrate that iron may be assimilated and built up into hæmoglobin only when it is absorbed in the form of an organic compound. Whether it is necessary that it should be received into the alimentary tract in the organic form, or whether it may be raised, by the process of digestion, from the inorganic to the organic combination and be absorbed and assimilated, was for a long time a debated question; but investigation has demonstrated that even in the form of a chloride the iron is raised to a peptonate or albuminate in the alimentary tract and absorbed.

Iron is an essential constituent of hæmoglobin. After it has served its purpose it may be excreted by the kidneys, by the epithelium of the intestines; even a small part is lost with the cuticle, hair, nails, etc.

(*j*) OTHER METALS are usually assimilated in chemical association with organic foodstuffs, and are excreted by the kidneys. A small amount of sodium, calcium, etc., is secreted by the pancreas and the liver, and is poured into the alimentary canal. A part of these metals is reabsorbed in combination as soap; all that is not reabsorbed is lost, in this way, to the organism.

6. THE CIRCULATION OF TYPICAL COMPOUNDS.

(*a*) WATER.—Our remote ancestry had undoubtedly an aquatic habitat. It has been said that, "man is, in a sense, an aquatic animal." It is true that about 60 per cent. of the body is water, that every active cell of the body is bathed in liquid and that even the surface of the body is, during health, usually covered with a film of moisture in the form of "sensible" or "insensible" perspiration. The organism can live many days without solid food, but deprivation of water for a very few days suffices to cause death.

The water is in part taken with the food and in part taken as drink. Water which is taken as such undergoes no change while in the system, except that an occasional molecule is joined by *Hydration* to some organic molecule. It is absorbed by the intestinal epithelium, even when it is taken between meals; when it is taken with a meal it is likewise passed on into the intestine with the chyme, to be absorbed by the intestinal epithelium. Water is the general solvent and diluent of the system. It makes possible the absorption of the digested foods and the excretion of waste products. Of all the water excreted by the kidneys, skin and lungs, a large part is water which enters the system as such; another part is the product of the oxidation of the hydrogen of the tissues in katabolism, while another portion has been released from complex molecules by dehydration, also a katabolic process.

(*b*) SODIUM CHLORIDE is taken as such with food. It is in solution in all the fluids of the body. It probably assists in endosmosis. It is probably the source of the chlorine element of the HCl of the gastric juice. (See "Secretion of HCl.") Sodium chloride may be formed in the system. It may be formed in the organism by a combination of absorbed hydrochloric acid with the carbonate or bicarbonate of sodium, as suggested under "*chlorine.*" It is excreted by the kidneys and skin and is secreted by lachrymal glands and salivary glands. It is in fact a constituent of every secretion and excretion.

(*c*) OTHER COMPOUNDS in this class are of not very great physiological importance.

7. THE CHARACTER OF THE METABOLIC CHANGES.

1. Association and Dissociation.

Hæmoglobin is associated with oxygen in the lungs and dissociated from oxygen in the tissue capillaries. Recent investigations indicate that the calcium phosphate of the milk is "associated" with one of the organic constituents, probably the casein, and that it retains this association through the steps of digestion and absorption possibly also to be assimilated in association with the foodstuffs. In bone and dentine, however, it is eventually dissociated and deposited as insoluble calcium phosphate. One or more molecules of water may be associated with another molecule in crystallization and dissociated when the crystal is dissolved or dehydrated.

2. Synthesis and Decomposition.

These terms are applied to a class of chemical changes which involves a more profound alteration in the structure of the molecule than that body undergoes in the preceding process (Association and Dissociation). The combination of a fatty acid with glycerine is a synthesis, while the breaking up of a fat into these two constituents is an example of a decomposition.

3. Hydration and Dehydration.

These terms signify the addition or subtraction of a molecule of water; it is only a specialized sort of synthesis or decomposition. Hydrolytic changes are especially common in the digestive process. Recall the addition of a molecule of water followed by a cleavage (hydrolytic cleavage) of the hydrated molecule into dextrine, and of a second molecule of water to maltose to make dextrose, while the dehydration of the same molecule of dextrose takes place in the liver, after absorption, reducing the dextrose to the amylose radicle ($C_6H_{10}O_5$), which taken n times is synthesized into a glycogen molecule $(C_6H_{10}O_5)_n$.

4. Reduction and Oxidation.

These terms need no explanation. In plants the reduction processes predominate and the liberated oxygen escapes into the general atmosphere. During reduction processes energy is used to consummate the change and energy is made latent. In the animal kingdom oxidation processes predominate; oxygen is taken from the atmosphere to consummate the change and carbon dioxide is returned to the atmosphere. Oxidation liberates latent energy.

SUMMARY: "*The chemical processes of the animal organism may be represented as a series of syntheses and decompositions, or of anabolic and katabolic changes, by virtue of which the highly complex and slightly oxidized constituents of the body and of foodstuffs are decomposed into simple and highly oxidized compounds, which are removed from the body by the various organs of excretion." The difference between the potentiality of the ingesta and the egesta represents the potential energy liberated in the organism as the kinetic energy of life.*

ANIMAL METABOLISM.

A. THE METABOLIC CHANGES OF DIFFERENT CLASSES OF FOODSTUFFS.

1. CARBOHYDRATES.

1. **Absorption Form.**—It will be remembered that during the process of digestion the carbohydrates are for the most part changed to dextrose. There is no evidence that other diffusible or even indiffusible carbohydrates may not be absorbed, *i. e.*, pass into the epithelium of the alimentary tract; all the carbohydrate matter found in circulation in the portal system is, however, dextrose. It is evident then that if cane sugar is absorbed by the epithelium, it undergoes hydrolytic cleavage in the epithelium and enters the circulation as dextrose; so that, in whatever form the carbohydrate is absorbed it is changed to dextrose by the epithelium and passed into the capillaries of the *portal system.*

2. **Circulation Form.**—In the blood all sugars normally appear as dextrose. The blood of the portal vein may have as much as 0.3 per cent., while that of the general circulation has usually about 0.1 per cent. Furthermore, the above mentioned high percentage for the portal circulation may be observed only after a meal rich in carbohydrates, while the amount quoted for the general circulation is more or less constant. The blood which enters the liver may have 0.3 per cent. dextrose, the blood which leaves uniformly has 0.1 per cent. dextrose. With these facts in view, it is evident that the liver must effect a profound change in the carbohydrate material brought to it by the portal system.

3. **Metabolism of Carbohydrates.**—The blood entering the liver after a meal brings a much larger amount of carbohydrate material than is carried away by the hepatic vein. That this excess of carbohydrates must be stored in the liver is the necessary conclusion; yet if a freshly excised liver be tested for dextrose that substance will not be found in greater quantity than

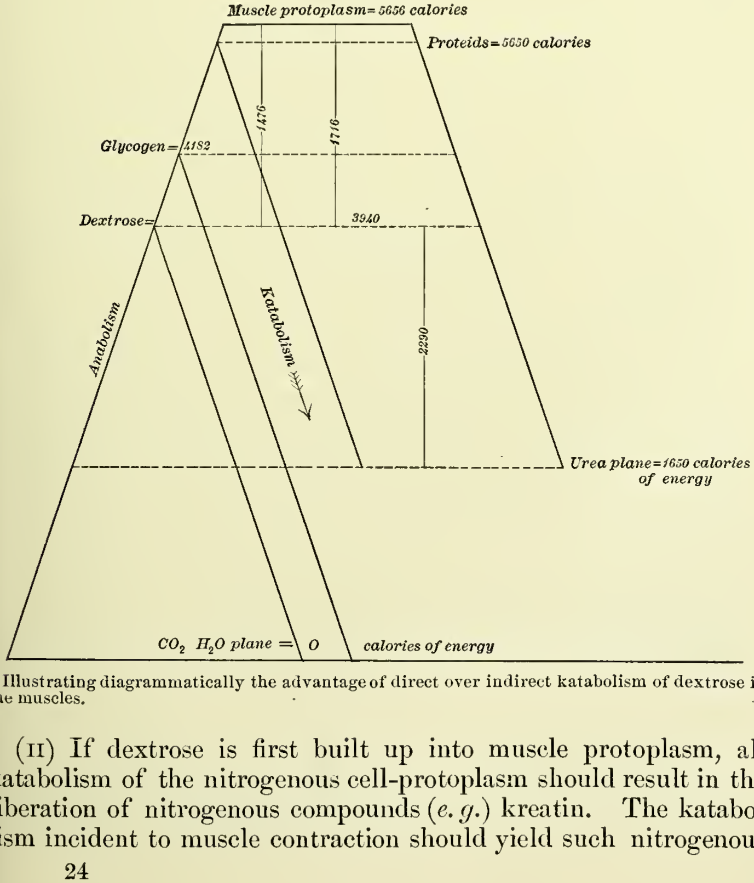
may be accounted for by the portal blood present. A special treatment reveals another form of carbohydrate—glycogen.

(*a*) GLYCOGEN $(C_6H_{10}O_5)_n$ was discovered and described by Claude Bernard in 1857. Bernard's theory as to its relation to general nutrition is substantially the one which is accepted to-day. Briefly outlined the preparation of glycogen is as follows: (*a*) Kill an animal after a heavy carbohydrate meal. (*b*) Excise liver, hash same and plunge it into boiling water, which has the double function of extracting glycogen and of stopping post-mortem change of glycogen to dextrose. (*c*) Filter. The opalescent filtrate contains glycogen or "animal starch." If one subject this animal starch to the iodine test a *wine-color* will result. The microscope reveals the presence of glycogen in liver cells, deposited in the substance of the cytoplasm. (See Fig. 193.) But the carbohydrates do not represent the sole source of glycogen; for an animal deprived of both carbohydrates and fats will still form glycogen in the liver on a pure proteid diet. Such is not the case, however, on a pure fat diet. Whether, with a mixed diet of carbohydrates and proteids, a part of the proteids are used in the formation of glycogen remains yet undetermined.

(*b*) TRANSFORMATION OF GLYCOGEN IN THE METABOLIC TISSUES.—In plants the starch formed in the chlorophyll grains of the leaves must be changed to a soluble form—dextrose, for example—before it can be carried by the circulatory system of the plant (fibro-vascular system) to distant parts of the plants for deposit, or for further metabolism. In animals the glycogen is only temporarily stored in the liver. It is to be used in the general metabolic tissues of the body—for the most part the muscles. It cannot be carried to the muscles in the insoluble form in which it is deposited in the liver. The liver possesses an amylolytic ferment which changes the animal starch to dextrose. In this soluble and diffusible form it enters the circulation, is carried to the metabolic tissues, absorbed or "selected" by the active cells of these tissues, and is by them metabolized. Just at this point we enter a controversial field. All are agreed that within the muscle cells the dextrose is subjected to a series of metabolic changes whose ultimate result is the liberation of energy. Some believe that before the foodstuff can yield to the animal organism its potential energy *it must be built up by the cell into living cell-protoplasm*. Others believe that the energy of the foodstuffs may be *directly* liberated without the necessity of a long series of anabolic changes preceding those katabolic changes which must finally liberate the energy. Here are certain facts which deserve consideration in this connection: (1) Glycogen is found in abundance in the muscle. Its source must be dextrose taken up from the blood by the muscle cells. But glycogen can be formed from dextrose only by the steps which represent *anabolic* changes. (Dehydration followed by recombination of *n* times the $C_6H_{10}O_5$ radicle into a glycogen molecule) The energy made latent in this anabolism is represented by 242 calories per gramme glycogen. To anabolize glycogen and nitrogenous foodstuffs into muscle protoplasm would require not less than 1476 calories of energy ; a total of about 1716 calories. The katabolism of muscle protoplasm yields 4000 calories per gramme muscle. The remaining 840 calories of energy is contained in the urea. The net gain in energy is represented by 2290 calories.

But the direct katabolism of dextrose would yield 3940 calories of energy. There would be a loss of 1650 calories, or about 41 per cent. of the energy of the foodstuff. Animals able to directly katabolize dextrose in the muscle cells would have an advantage over those not having that ability. (See Fig. 196.)

FIG. 196.



Illustrating diagrammatically the advantage of direct over indirect katabolism of dextrose in the muscles.

(II) If dextrose is first built up into muscle protoplasm, all katabolism of the nitrogenous cell-protoplasm should result in the liberation of nitrogenous compounds (*e. g.*) kreatin. The katabolism incident to muscle contraction should yield such nitrogenous katabolites in proportion to the muscular energy expended. But these nitrogenous katabolites are further changed and appear in the excreta as urea, CO_2 and H_2O. The urea then should be a measure of muscular work; but urea does not essentially vary with varying muscular activity. The hypothesis that the dextrose is anabolized to the plane of cell protoplasm is not in harmony with the facts of excretion and the evidence is strong against the hypothesis. (III) If dextrose may be directly katabolized from the dextrose or from the glycogen plane the katabolites CO_2 and H_2O should vary with muscular activity. The excretion of CO_2 and H_2O varies directly with muscular activity. This is in harmony with the facts of excretion and is strong evidence in its favor.

4. **The more Permanent Deposit of Carbohydrates.**—That this occurs not in the form of carbohydrates but in the metabolized form of fat has been demonstrated. A part of the carbohydrate foodstuff in circulation as dextrose is absorbed by living connective tissue cells and transformed into fat which is deposited in the cells and held as a reserve of potential energy to be called out when the more easily metabolized glycogen and dextrose are insufficient for the needs of the system. What is the character of the change the dextrose molecules must undergo to make palmitin? We know that palmitic acid is readily synthesized with glycerine to form tri-palmitin. The storage of fat must involve the following general changes:

(I) 3 × Palmitic acid $= 3[CH_3(CH_2)_{14}\cdot COOH] = 3[C_{16}H_{32}O_2] = C_{48}H_{96}O_6$.

(II) 8 × Dextrose $= 8[C_6H_{12}O_6] = C_{48}H_{96}O_{48}$.

(III) 8 Dextrose + Glycerol = Tri-palmitin + $3H_2O + 42O$.

The formation of fat from dextrose must be attended by the liberation of oxygen. This is an anabolic process to consummate which requires energy amounting to about 5500 calories per gramme fat. That it takes place in one reaction as written above is not probable. That it is eventually a combination of *dextrose* and *glycerol* is an undemonstrated hypothesis. *That the process whatever it may be is an anabolic one attended with the liberation of oxygen and the making latent of energy is beyond question.*

5. **Excretion of Carbohydrate Katabolites.**—The katabolism of carbohydrates yields CO_2 and H_2O. These waste materials are excreted by the lungs, skin and kidneys unchanged or recombined but for the most part unchanged.

2. PROTEIDS.

1. **Absorption Form.**—Most proteids enter the epithelium from the alimentary canal as peptones and proteoses. A small portion may enter as acid-albumin or alkali-albumin or even native

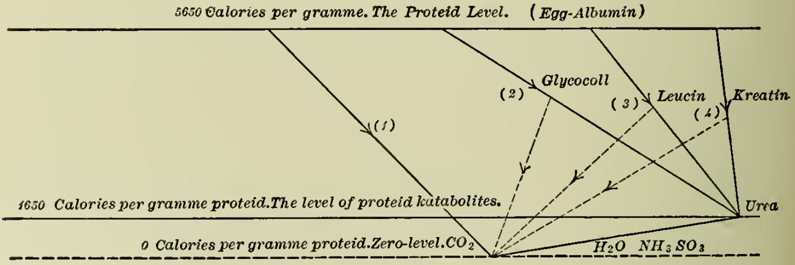
proteid. Within the epithelium these proteids undergo a change. Evidence of this is cited in the facts that neither peptone nor proteose is found in either blood or lymph ; and that when injected into the circulatory system is promptly excreted as such. The living cells of the intestinal epithelium must be able therefore to transform the proteids absorbed into the normal proteids of the circulation. This combination consists in a recombination of simple nitrogenous molecules into more complex ones with liberation of water.

2. **Circulation Form.**—The blood contains plasma-proteids,—serum albumin and serum globulin,—and corpuscle proteids. There can be no doubt that the absorbed proteid foodstuff enters the plasma, increasing its quantity of one or both proteids. There is no storehouse for reserve proteids except so far as the circulation itself serves such a purpose. The *absorbed proteid,* transformed through the metabolic activity of the cells of the intestinal epithelium into serum albumin and serum globulin *is received by the portal system* and thence distributed to the system as constituents of blood-plasma, lymph-plasma, and tissue-plasma. Every living cell of the system may select from the plasma which bathes it such variety and quantity of the plasma proteids as are necessary in carrying on the cell activities.

3. **Metabolism of Proteids.**—As in the case of carbohydrates, so here, the question as to whether or not all katabolism of proteids proceeds from living cell-protoplasm is a controversial one. Many of the cytologists would answer the question affirmatively. There are strong indications amounting almost to a demonstration, that only a part of the proteid is anabolized to the plane of living cell-protoplasm while a part is directly katabolized. Among the considerations favoring the second position one may mention : (I) The correspondence of proteid katabolism rather to the variation of proteid consumption than to special cell activity. This is especially marked in the case of the muscle-metabolism and will be treated later. (II) Albuminoids—*e. g.*, gelatin—can not be built up into tissue though they may be used as energy-producing nitrogenous foods.

The preponderance of evidence in favor of the view that not all proteids are first raised to the plane of living protoplasm before being katabolized leads to the division of the proteid supply into two parts: (I) Tissue-producing proteids ; (II) energy-producing proteids. This division corresponds roughly to Voit's classification into "organ proteid and circulating-proteid." It is now believed that *all metabolic changes are intracellular,* so that Voit's terms seem less appropriate than the terms suggested above. The tissue proteid is that portion of the nitrogenous foodstuff which is built up by the cells into *living protoplasm.* The energy-producing proteid is that portion which is directly katabolized *within the cell under the influence of the living protoplasm,*—and serves the sole purpose of producing energy. It must not be forgotten that the tissue proteid in its final katabolism incident to the special activity of the cell yields energy also. Whether one follows the changes of tissue proteids or of energy-producing proteids he eventually considers the decomposition—direct or indirect—of a nitrogenous foodstuff from the proteid level to the urea level. In general proteids represent 5650 calories per gramme proteid while the unavailable energy of a gramme of proteid represents 1650 calories (Rubner); the net energy represented by one gramme of proteid material being about 4000 calories. Much remains yet to be determined regarding the specific changes which the proteid undergoes in this decomposition. This much is known: (I) Some of the proteid is reduced to CO_2, H_2O, NH_3, etc., and these in part recombine, forming urea in which NH_3 is combined with C, O, and H; (II) some of the proteid is changed more directly to urea; glycocoll, leucin, kreatin, and sarcolactic acid being mid-products of the katabolism. Hofmeister's[1] formula for albumin will give us some idea of the complexity of a typical proteid: $C_{204}H_{322}N_{52}O_{66}S_2$. Hill's diagram (Fig. 197) represents graphically the relation between proteid and urea.

FIG. 197.


5650 Calories per gramme. The Proteid Level. (Egg-Albumin)
(1)
(2)
Glycocoll
(3)
Leucin
(4)
Kreatin
1650 Calories per gramme proteid. The level of proteid katabolites.
Urea
0 Calories per gramme proteid. Zero-level. CO2
H2O NH3 SO3

(*a*) Letting the egg albumin represent the proteids we see that 431 atoms of oxygen will oxidize one molecule of the albumin to $204CO_2 + 83H_2O + 52NH_3 + 2SO_3$. But these elementary compounds are in part recombined before excretion. Nascent NH_3 radicles combine instantly with CO_2 and H_2O to make ammonium carbonate: $O = C \begin{matrix} -OH + NH_3 \\ -OH + NH_3 \end{matrix} = O = C \begin{matrix} -ONH_4 \\ -ONH_4 \end{matrix}$, the ammonium carbonate is dehydrated to form ammonium carbamate, and again dehydrated to form urea:

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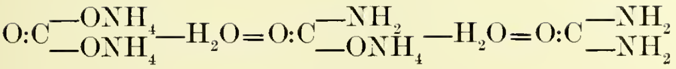
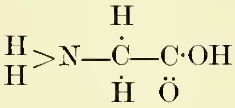
[1] *Zeitsch. f. phys. chem.*, Bd. 16, S. 187. Quoted by Bunge, Physiol. Chem., 1894, p. 55.



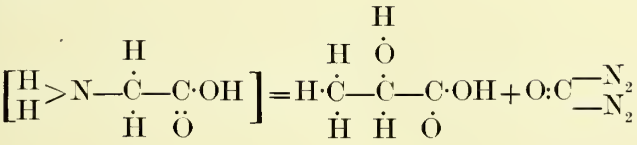
$$O{:}C\begin{matrix}-ONH_4\\-ONH_4\end{matrix}-H_2O=O{:}C\begin{matrix}-NH_2\\-ONH_4\end{matrix}-H_2O=O{:}C\begin{matrix}-NH_2\\-NH_2\end{matrix}$$

(*b*) *Glycocoll* (or Glycin, or Amido-acetic acid)



$${}^{H}_{H}\!>N-\overset{H}{\underset{H}{\dot{C}}}-\underset{\ddot{O}}{C}\cdot OH$$

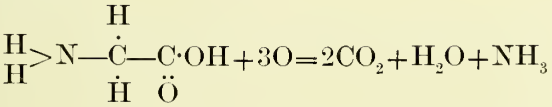
I Direct :



$$\left[{}^{H}_{H}\!>N-\overset{H}{\underset{H}{\dot{C}}}-\underset{\ddot{O}}{C}\cdot OH\right]=H\cdot\overset{H}{\underset{H}{\dot{C}}}-\overset{\overset{H}{\dot{O}}}{\underset{H}{\dot{C}}}-\underset{\dot{O}}{C}\cdot OH+O{:}C\begin{matrix}-N_2\\-N_2\end{matrix}$$

2 Glycocoll=Sarcolactic acid+urea.

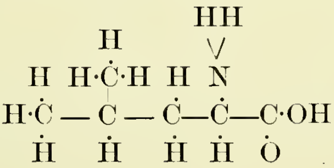
II Indirect :



$${}^{H}_{H}\!>N-\overset{H}{\underset{H}{\dot{C}}}-\underset{\ddot{O}}{C}\cdot OH+3O=2CO_2+H_2O+NH_3$$

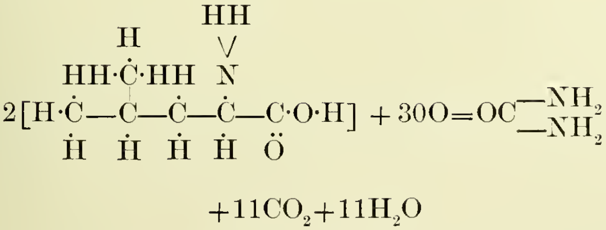
which may recombine, as in the case of albumin, to form urea.

(*c*) *Leucin* or Iso-butyl-amido-acetic acid:



$$H\cdot\overset{H}{\underset{H}{\dot{C}}}-\overset{\overset{H}{H\cdot\dot{C}\cdot H}}{\underset{H}{C}}-\overset{H}{\underset{H}{\dot{C}}}-\overset{\overset{HH}{\vee}}{\overset{N}{\underset{H}{\dot{C}}}}-\underset{\dot{O}}{C}\cdot OH$$

(I) Direct :



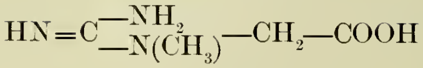
$$2\left[H\cdot\overset{H}{\underset{H}{\dot{C}}}-\overset{\overset{H}{H\cdot\dot{C}\cdot H}}{\underset{H}{\dot{C}}}-\overset{H}{\underset{H}{\dot{C}}}-\overset{\overset{HH}{\vee}}{\overset{N}{\underset{H}{\dot{C}}}}-\underset{\ddot{O}}{C}\cdot O\cdot H\right]+30O=OC\begin{matrix}-NH_2\\-NH_2\end{matrix}$$

$$+11CO_2+11H_2O$$

2 Leucin plus oxygen=urea, carbon dioxide and water.

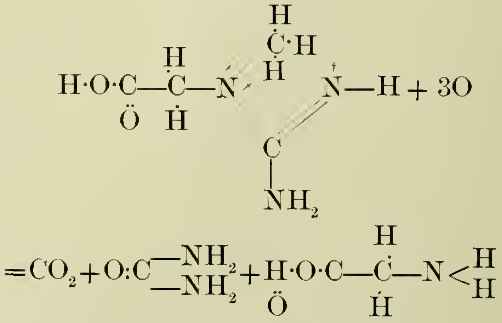
(II) Indirect : Leucine + 15O = $6CO_2$ + $5H_2O$ + NH_3. Leucin plus oxygen = carbon dioxide, water, and ammonia.

(*d*) *Kreatin* or methyl-guanidin-acetic acid,



$$HN{=}C\begin{matrix}-NH_2\\-N(CH_3)\end{matrix}-CH_2-COOH$$

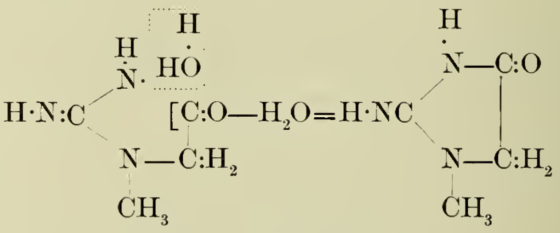
(I) Direct :



Kreatin plus oxygen $=CO_2$, urea and glycocoll.

(II) Indirect : Kreatin $+6O=3NH_3+4CO_2$.

(III) It is possible that in kreatin we have the most important preliminary katabolite of muscle protoplasm. It is found in considerable amount in muscle; it is therefore ingested with lean meat. But experiment shows that ingested kreatin follows a course of katabolism different from that formed in the muscles, namely that it is dehydrated in the liver and excreted by the kidneys as kreatinin.



Kreatin minus water=Kreatinin.

But the kreatin which is formed in the muscle is also transformed there; that is, kreatin represents a preliminary katabolite which is further katabolized in the muscle. Small amounts of glycocoll and considerable amounts of sarcolactic acid are found in the muscles. When glycocoll or sarcolactic acid or ammonium lactate is introduced into the system it is promptly changed in the liver to urea, CO_2 and H_2O. Glycocoll may, however, be combined with members of the benzole series (see Hippuric acid under anabolism).

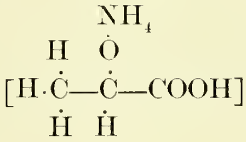
The observations of Gaglio, V. Frey, Marfori, Minkowski and others (quoted by Schaefer, Text-book of Physiology, Vol. I., p. 905) make it certain: (1) that sarcolactic acid is formed in various metabolic tissues; (2) that it circulates in the form of an acid or ammonium salt in the blood; and (3) that it is changed in the liver to urea and certain by-products.

There is no positive proof that kreatin is a forerunner of sarcolactic acid. The probabilities are favorable to such a relation. The course of katabolism may, in the light of recent work in this field, be assumed to be something as follows:

(I) *Kreatin* + 3O = CO_2 + UREA + *glycocoll.*

(II) Glycocoll = UREA + *sarcolatic acid* (CH_3—CHOH—COOH).

(III) Sarcolactic acid + NH_3 = *Ammonium lactate*



$$[\mathrm{H}\cdot\underset{\mathrm{H}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\overset{\mathrm{NH_4}}{\mathrm{O}}}{\mathrm{C}}}-\mathrm{COOH}]$$

(IV) 2 Ammonium lactate + 12O = $5CO_2$ + $5H_2O$ + *Ammonium carbonate.*

(V) Ammonium carbonate—H_2O = *Ammonium carbamate.*

(VI) Ammonium carbamate —H_2O = UREA.

NOTE: (1) That the series of changes suggested here represent a *step by step* process by which a complex body is reduced to a series of simple bodies; (2) that the processes are, with one exception (III), oxidations, dehydrations and decompositions.

Where do these problematic changes take place? As is already indicated above, the kreatin of the body has two sources.

A part comes from the ingested lean meat and is dehydrated in the *liver*, forming kreatinin; a part is formed in the muscles and is probably changed at once to urea, CO_2 and glycocoll, or possibly directly to sarcolactic acid, urea and CO_2. In either case the products of katabolism which enter the circulation are sarcolactic acid and the elements of urea, or, more likely, ammonium lactate and ammonium carbonate.[1]

Ammonium lactate and ammonium carbonate brought to the liver are promptly subjected to the changes indicated in equations (IV), (V) and (VI).

As with kreatin so with leucin, there are two sources in the system of an omnivorous or a carnivorous animal: (I) From the alimentary tract where leucin is a product of trypsin decomposition of peptone. A part of the leucin so formed is absorbed and carried to the liver in the portal circulation. (II) But aside from this source leucin is one of the mid-products of normal proteid katabolism and is found in small amounts in all liquids of the body. In due time it makes its journey to the liver with the general circulation, and in that organ is further katabolized to its simpler elements, and is excreted as urea, CO_2 and H_2O.

---

[1] We can imagine that the products of reactions (III) and (IV); or possibly the products of a hydrolytic cleavage of kreatin pass into the circulation. Thus:

Kreatin + $4H_2O$ = Ammonium lactate + Ammonium Carbonate.

That the liver is seat of this change is practically demonstrated by the observation that when the liver becomes extensively diseased leucin accumulates in the blood to a more than normal degree and is finally excreted unchanged by the kidneys.

Glycocoll or glycin may be considered a normal mid-product of proteid katabolism, and if a dog be fed benzoic acid he will excrete, via the kidneys, hippuric acid which is a combination of benzoic acid and glycocoll. This indicates that the glycocoll must have been furnished by the system. That it was furnished for this particular purpose is not probable. Without much chance of error we may assume that the glycocoll used by the dog's liver in the above mentioned case was present as a normal constituent of the blood and that had not the benzoic acid from the portal circulation been brought into relation with the glycocoll it would have been katabolized *in the liver* to the urea plane either directly or indirectly. This is confirmed by the observation that when glycocoll is fed to a dog it appears in the urine as urea—having been changed *in the liver*. We may thus sum up the answer to the questions which introduced this paragraph: (I) *The early steps in proteid katabolism take place in the various metabolic tissues, principally the muscles,*—though the alimentary tract is the scene of certain preliminary changes and some changes may be wrought in the blood itself. (II) *The final steps of proteid katabolism take place in the liver.*

4. **The Nutritive Value of Proteids.**—Preliminary to a discussion of this topic it will be necessary to define two expressions which have much significance in physiology.

(*a*) NITROGEN EQUILIBRIUM is an expression signifying the *balance* of *nitrogen* INCOME and OUTGO. It means that the nitrogen which the body loses in the excreta—principally in the urea in man—is just covered by the nitrogen received in the proteid foods. If the excreted nitrogen is in excess of the ingested nitrogen it must be evident that the excess must have come from the nitrogen supply of the system. For a very short time this excess might be furnished by katabolism of energy-producing proteids. But at longest a few days would suffice to expend all the available reserve of proteid in blood, lymph plasma and tissue plasma; and the excess would then be drawn from the living active cells of muscles, glands and nervous system. The organism gives up this life balance very reluctantly and under such circumstances the proteid excretion is reduced to a minimum. On the other hand, when the ingested nitrogen is in excess of the excreted nitrogen the balance is in favor of the organism. It might at first be expected that the system would guard this credit very carefully and store it away in increased volume of living tissue, *e. g.*, increased muscle tissue, increased gland tissue and increased nerve tissue. Under two conditions and under definite limitations this may be true. First, the growing animal utilizes a part of the nitrogenous balance to build up new tissues. Second, after a period of starvation —negative nitrogen balance—the emaciated living tissues will utilize a large part of the positive nitrogen balance, when the tide turns, to build up and reconstruct the wasted tissues. In both of these cases, however, when the normal growth or condition is reached an excess is not utilized to build up more muscle or more brain, but the system uses it day by day in *increased proteid metabolism*, thus balancing increased income by increased excretion. *The normal animal with a sufficient diet maintains a nitrogen equilibrium.*

(*b*) CARBON EQUILIBRIUM signifies a balance of income and outgo of carbon in food and excretions. Excess of carbon against the organism is an index of a draft on carbonaceous tissue. All tissues are carbonaceous, but not all tissues are necessarily drawn upon to furnish the carbon for increased katabolism. The carbon reserve in the deposited fats usually furnishes the balance. On the other hand a carbon-balance in favor of the system is usually deposited as fat. A negative nitrogen balance may exist at the same time that there is a positive carbon balance. Under such circumstances the animal might increase in weight at the same time that its muscle tissues are wasting through lack of sufficient proteid. A positive nitrogen balance and a negative carbon balance may exist together and yet the animal may increase in weight.

We may now discuss the nutritive value of proteids. The usual method of solving such questions is to institute two experiments: 1st, deprive the animal of the foodstuff in question; 2d, furnish the animal with no other than the one under consideration, meantime watching the progress of metabolism. This method, though open to the objection that so radical a change may not leave the animal in a really normal condition, has yielded some very important results. Pettenkoffer and Voit kept a 30-kilogram dog in nitrogen and carbon equilibrium on 1500 grammes of lean meat per day. By increasing the amount to 2500 grammes per day the animal maintained nitrogen equilibrium and laid on fat. Pflüger kept a dog in weight-equilibrium for a period of eight months on a lean meat diet. That the weight remained the same for so long a period is sufficient proof that the nitrogen equilibrium and the carbon equilibrium were both maintained. These experiments demonstrate that the carnivorous animal may get all of its required tissue material and energy-producing material from a pure proteid diet. Just how far this could be shown to hold for omnivorous or herbivorous animals has not been determined. There is no reason to doubt that if the proteid could be presented in a palatable form the results would be practically the same in these animals as in the carnivora. One may safely assume then that ingested proteid may be used by the system. (I) immediately in a series of katabolic processes which liberate the energy for the life processes; (II) as the nitrogenous factor in the building up of protoplasm; (III) as the carbon and hydrogen factors in the formation of fat. The term proteid as here used is intended to include all nitrogenous foods.

One class of proteids—the albuminoids, does not conform completely to the statement just made for proteids in general. The albuminoids, of which gelatin is an example, can not be built up into living cell protoplasm. Experiment shows that an animal will die about as quickly when kept on a carbohydrate, fat, and gelatin diet as when kept on a carbohydrate and fat diet. The gelatin can be immediately oxidized and may be substituted for a part of carbohydrate or fat, but it can not be built up into living protoplasm. In other words the albuminoids seem to be able to play the rôle of energy-producing proteids, but not of tissue-forming proteids. The relation of the albuminoids to nutrition seems to be in harmony with the hypothesis that only a part of the nitrogenous food is actually built up into living protoplasm, while the rest is katabolized from the proteid level, direct. This is, in fact, one of the strongest confirmatory considerations and amounts almost to a demonstration of the tenability of the hypothesis. In summing up one may say that *the proteids furnish the material necessary* (I) *for the rebuilding of cell protoplasm;* (II) *for direct nitrogenous katabolism;* (III) *for deposit as reserve fat;* and finally, (IV) this foodstuff may *take the place of a part of the carbohydrate*, a pure proteid diet actually furnishing material for glycogen and dextrose in the normal relations if somewhat less in quantity.

5. **The Laws of Nitrogen Equilibrium.**—When an animal receives a scanty supply of proteid in a mixed diet the organism economizes its tissue proteid as well as its energy-forming proteid by using carbohydrates and fats for energy production, even if need be drawing upon the reserve fat of the system for this purpose. There is a certain minimum beyond which the proteid can not be reduced without disturbing nitrogen equilibrium, for there is always some katabolism of living protoplasm and if the organism is not receiving proteid sufficient in quantity and proper in quality to replace this waste there will be more nitrogen egested than ingested.

When an animal receives an abundant supply of proteid in a mixed diet the organism seems to katabolize the usual amount of tissue-proteid and to draw freely upon the energy-producing proteid for the production of energy. If the quantity of carbohydrates and fat is sufficient to admit of it a portion of the food supply is stored as fat. Whether this stored fat comes from ingested fat, from carbohydrates or from proteids is a matter still in controversy. In either case the proteid is so far katabolized as to release the nitrogen which immediately finds its way to the egesta as urea or related nitrogenous excreta. From this it appears that with small nitrogenous ingestion there is small nitrogenous egestion, while with abundant nitrogenous ingestion there is correspondingly increased nitrogenous egestion. In general, then:

(*a*) LAW I, *the katabolism of proteids varies with the supply of proteids*, nitrogenous equilibrium being maintained within comparatively wide limits of supply.

(*b*) LAW II. *The katabolism of proteid is nearly independent of muscular work.*

(*α*) *Liebig's Theory.* Liebig believed: (I) that all assimilated proteid is built up into living protoplasmic tissues; (II) that every manifestation of life,—muscular contractions, secretion, thought—is the result of a breaking down of living tissues; (III) that this katabolism of protoplasm releases nitrogen or nitrogen compounds which found their way more or less directly to the excreta; and (IV) that the quantity of nitrogen in the excreta is a measure of the katabolic activity. This theory is so reasonable that it stood unassailable for a considerable period. If it is in harmony with the facts of nutrition one would expect a marked variation of the quantity of nitrogen elimination following muscular work.

(*β*) *Experiment of Fick and Wislicenus.* These two young men, who later attained world-wide renown and recognition as physiologist and chemist, respectively, put Liebig's theory to a practical test. After using a non-nitrogenous diet for a period of seventeen hours, they began the ascent of the Faulhorn, whose summit they reached after eight hours of the most fatiguing muscular exertion, having lifted their bodies through a vertical distance of 1956 meters. Fick weighed 66 kilogrammes, he had performed 129,096 kilogram-meters of work in climbing, meantime the heart and respiratory muscles had performed work which was estimated to amount to about 30,000 kilogram-meters, making a total of 160,000 kilogram-meters of energy of muscular contraction. During the climb and six hours subsequent to it the non-nitrogenous diet was continued. During the whole observation period of thirty-one hours the renal excretion was periodically taken and kept for analysis. If Liebig's theory were tenable then the nitrogen excretion during and subsequent to the climb should have been much increased because muscle katabolism was much increased. But analysis showed *no essential increase of the nitrogen elimina-*

tion! The result of this experiment was generally accepted as conclusive that the Liebig theory is untenable. Voit and Pettenhoffer subjected a dog to alternating days of rest and hard work in a treadmill. The chemical analysis of the excreta showed that the nitrogen metabolism is practically the same on work days as on rest days. The experimenters then made a similar test upon a man, who alternated rest with work in a respiratory chamber. It was found that *nitrogen excretion,* and therefore proteid katabolism, *is practically independent* of *muscular contraction.* Care has been taken not to leave the impression that proteid metabolism is independent of katabolism in muscle tissue; katabolism in muscle tissue progresses while the muscles are at perfect rest; *i. e.,* while no contractions are occurring. This *rest-katabolism* of muscle tissue liberates heat energy. This process involves the activity of living muscle protoplasm, and there is no reason to doubt that incident to this heat production and incident to contraction a certain amount of living protoplasm is katabolized, and this certain amount seems to be practically the same whether the muscle protoplasm expresses its energy in the form of mechanical work or in the form of heat. In either case the muscle cells seem to be able to utilize absorbed dextrose and the energy-producing proteids in this energy liberation. Whether the energy to be liberated is heat energy or mechanical the carbohydrates can be used as well as the circulating proteid, so that with sufficient and uniform food there will be a nearly uniform nitrogen excretion, any variations being independent of the variations of mechanical energy liberated.

Relation of non-nitrogenous metabolism to muscular work. The experiments of Voit and Pettenhoffer with men and animals in respiratory chambers demonstrate that the energy of muscular work, *under normal conditions, comes mainly, if not exclusively,* from the oxidation of non-nitrogenous material.

3. FATS.

1. **Absorption Form.**—Fats are absorbed in the form in which the digestive processes have them,—named in the order of their relative quantities: (I) Fatty Acids and glycerol, (II) Soaps, (III) Emulsions.

2. **Circulation Form.**—One would seek in vain for either fatty acid, glycerol or soap in the portal system as well as in the lacteals. If fatty acid be fed to a dog it will appear in the lacteals as fat in emulsion. To *absorbed fatty acid glycerol is joined* to make a fat which enters the lacteals in minute subdivision—an emulsion—which is emptied by the thoracic duct into the general circulation.

3. **Metabolism of Fats.**—The fat of each species possesses a particular proportion of the three components: Palmitin, Stearin, and Olein. If a dog be fed on lean meat plus palmitin plus olein in sufficient quantities he will lay on fat; analysis of this fat will show that it is a typical dog-fat having the usual proportion of stearin. From such an experiment one must conclude that the dog has the power to change either palmitin or olein into stearin, or that he has the power to form stearin from proteid. As above cited the dog may lay on typical fat on a pure proteid diet. It is then certain that the stearin may have been formed from the proteid and not from other fats and if the stearin why not the others, also? Is there anything to prove that all of the fat was not directly katabolized to furnish the immediate source of energy and that proteid was the source of all the fat? No, and such may have been the case. Another experiment, however, proves that a foreign fat, rape oil, may be deposited unchanged. If such is the case with a foreign fat may it not also be true of those varieties of fat found normally in the body of the animal under consideration? This is believed to be the case. It is believed that *excess of fat may be deposited as reserve.* Regarding that which is katabolized immediately little is known as to the location of the katabolism. It may be oxidized in the blood; it is more likely that it is oxidized in the metabolic tissues. In any case the end products are CO_2 and H_2O and these katabolites are excreted by lungs, skin and kidneys. In the anabolism of fatty acid and glycerine little energy is made latent. In the katabolism of fat to its end products CO_2 and H_2O a relatively large amount of energy is liberated. The calorimeter shows that one gramme of pure fat will liberate about 9400 calories of energy on oxidation. This is much more than is liberated by the same amount of proteid. There are 155 atoms in a molecule of tri-palmitin, whose oxidation requires 145 atoms of oxygen. There are 644 atoms in a molecule of albumin whose oxidation requires 431 atoms of oxygen. If the relative amount of oxygen required to be taken as an index of the energy liberated then the fat would have about 1.5 times the amount of energy represented by the albumin. It has nearly 1.7 times the energy of albumin, which fact is probably due to difference in molecular constitution, *i. e.*, in the relative amounts of CO_2, H_2O, and NH_3 formed on oxidation.

4. **Fat Deposit.**—(*a*) *From the carbohydrates of the food* (see carbohydrates). (β) *From the proteids of the food.*—Proteid contains 15 per cent. of nitrogen and 50 per cent. of carbon. Urea contains 46 per cent. of nitrogen and 20 per cent. of carbon.

From this it follows that less than $\frac{1}{7}$ of the carbon of proteid will be eliminated with the urea which carries off all the nitrogen.

From this carbonaceous residue the organism seems able to build up fat. In an experiment upon a dog which was in nitrogen equilibrium a pure proteid food containing 68 grammes nitrogen and 250 grammes carbon was given. When 67.9 grammes of nitrogen had been eliminated only 207 grammes of carbon had been eliminated. There was a balance of 43 grammes of carbon retained and laid on as fat; 58 grammes representing 17 per cent. of the total carbon. (γ) *From the Fats of the Food.*—It was formerly supposed that much of the deposited fat came from the ingested fat. It is clear in the light of recent investigation that at most only a small portion of it has this source.

4. THE INTERRELATIONS OF THE FOODSTUFFS.

The following figure (Fig. 198) affords a graphic illustration of the interrelations which have already been discussed.

FIG. 198.

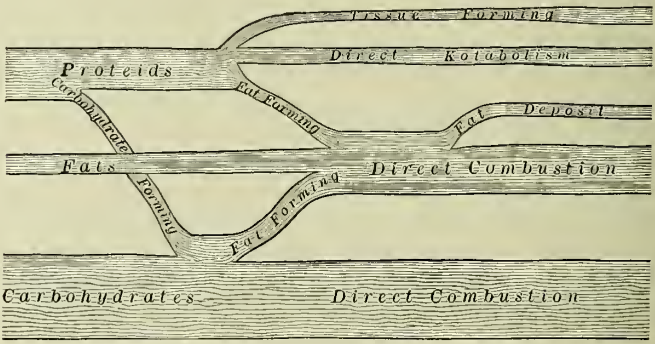


Diagram illustrating the interrelation of the foodstuffs.

B. SUMMARY OF ANABOLISM AND KATABOLISM.

1. ANABOLISM.

Frequent reference has been made to anabolism and many anabolic changes have been given. It is proposed here to enumerate these, explaining such as have not already been discussed.

(*a*) The synthesis of fatty acids and glycerol in the epithelium of the alimentary tract.

(*b*) The synthesis of *n* molecules of dextrose with dehydration of same to form glycogen in the liver and in the muscles.

(*c*) The recombination of peptone molecules into serum albumin and serum globulin in the epithelium of the villi.

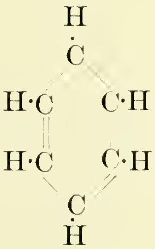
(*d*) The synthesis of carbohydrates to form fat for deposit in adipose tissue. This process is accompanied by liberation of oxygen.

(*e*) The anabolism of proteid foodstuff, or blood proteids into living protoplasm.

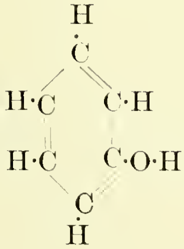
(*f*) *Synthesis of Phenol with Sulphuric Acid.*

Phenol differs from benzole in the replacement of one of the hydrogen atoms by the OH radical.

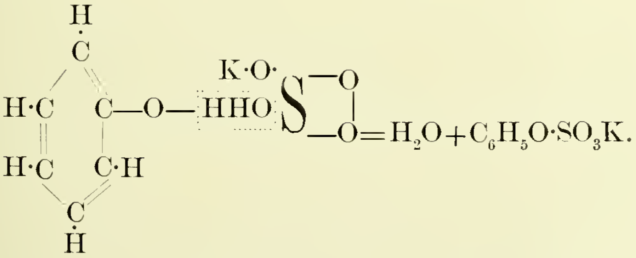
Benzole :



; Phenol :



Benzole, phenol, and benzoic acid are frequent constituents of the products of digestion and of urine. Benzoic acid given with the food appears in the urine in some derived form brought about by a synthesis. The reaction may be represented by the following equation :



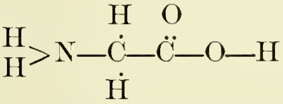
$= H_2O + C_6H_5O \cdot SO_3K.$

Phenol + Acid Sulphate of Potassium = Water + Phenol-Sulphate of Potassium.

(*g*) *Synthesis of Benzoic acid with glycocoll.*

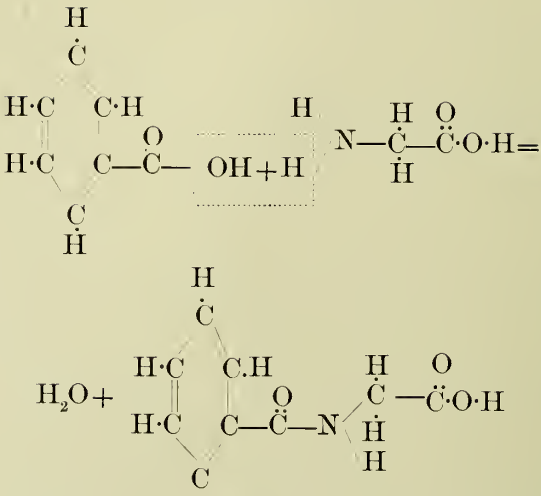
Benzoic acid differs from phenol in the substitution of the COOH radical in the place of the OH. Glycocoll or amidoacetic acid is formed from acetic acid by the substitution of NH_2 for H thus :

Glycocoll : or glycin :



$$\begin{matrix}H\\H\end{matrix}\!>N-\overset{H}{\underset{H}{C}}-\overset{O}{C}-O-H$$

The synthesis takes place with the liberation of a molecule of water and the formation of one molecule of hippuric acid, a constant but not an important constituent of urine :



Benzoic acid+Glycin=Water+Hippuric acid or Benzamido acetic acid.

2. KATABOLISM.

The cases already discussed will simply be enumerated here.

(*a*) The hydrolytic cleavage of dextrine molecules by the cells of the intestinal epithelium with the formation of dextrose.

(*b*) The hydrolytic cleavage of glycogen into *n* molecules of dextrose for each molecule of glycogen. This takes place in the liver and in the muscles.

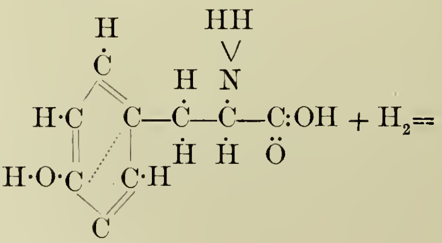
(*c*) The formation in metabolic tissues of such mid-products of katabolism as kreatin, leucin, tyrosin, glycocoll, etc.

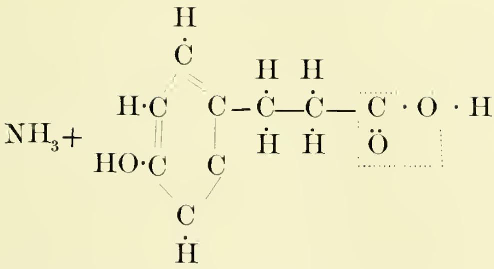
(*d*) The formation in the metabolic tissues of such secondary products of katabolism as sarcolatic acid, ammonium lactate, ammonium carbonate, etc.

(*e*) The formation, in the liver, of such end-products of katabolism as urea, CO_2, H_2O.

(*f*) *The katabolism of tyrosin.*

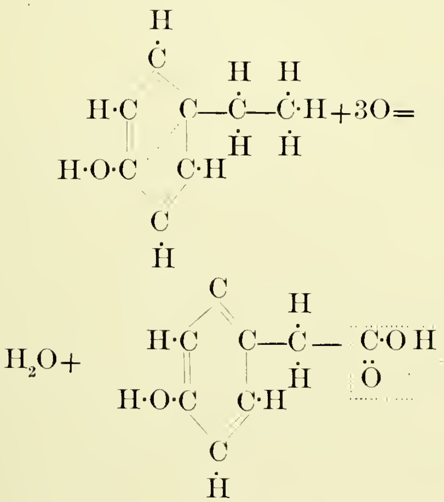
(I) Tyrosin or p-oxy-phenyl-amido propionic acid$+H_2=NH_3$ +p-oxy-phenyl-propionic-acid or p-hydro-cumaric acid. Thus:





(II) Para-oxy-phenyl-propionic acid—CO_2=para-ethyl-phenol.

(III)



Para-ethyl phenol + 3O = H_2O + para-oxy-phenyl-acetic acid.

(IV) Para-oxy-phenyl-acetic acid − CO_2 = para-methyl-phenol or para-cresol.

(See formula under (III) for indication of the change.)

(V) Para-methyl-phenol +3O = H_2O+ para-oxy-benzoic acid.

(VI) Para-oxy-benzoic acid — CO_2 = phenol.

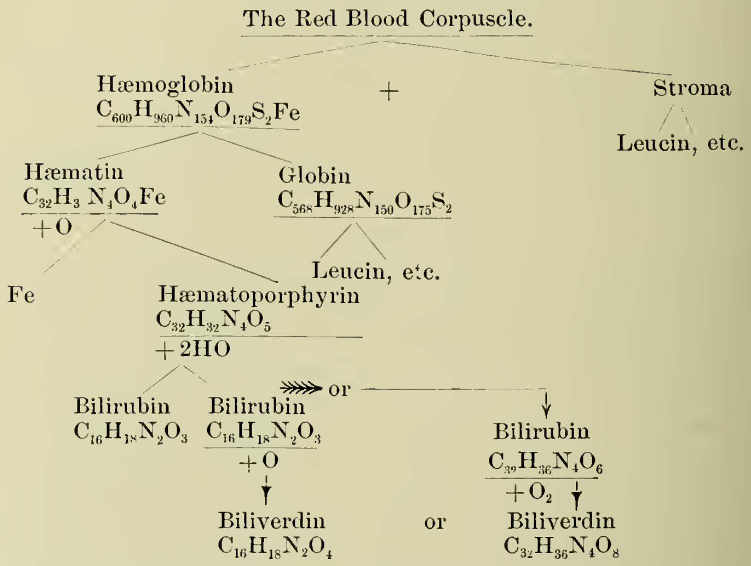
These last steps in the process take place in the manner indicated in the earlier steps.

Phenol is absorbed and as we have seen above may be synthesis with acid sulphate of potassium.

(*g*) *The katabolism of the red blood corpuscle.* The very great importance of the red blood corpuscle, in its relations to the general organism, justifies the discussion of its katabolism at some length, though our knowledge of this process is somewhat fragmentary. The *red blood* corpuscle has a limited period of activity. At the end of that period the physical union between the hæmoglobin and the stroma of the corpuscle is dissolved.

There is not sufficient evidence, either from histological or from chemical investigations, to warrant us in saying that the "breaking down" of the corpuscle occurs in the liver; it may occur in the liver or in the red marrow of bones—it *does occur in the spleen.* The débris of red blood corpuscles may always be found in the spleen, either in spleen cells or in leucocytes. Whether the senile red blood corpuscle is caught in the spleen pulp and incidentally engulfed by leucocytes or whether it is caught in the general circulation by the leucocytes and brought to the spleen is not known—probably both methods occur.

The following diagram indicates in a general way the steps in the katabolism of the red blood corpuscles.



We may sum up the katabolism of the red blood corpuscle by saying that it is broken up into biliverdin, bilirubin, iron and a series of such bodies as leucin which are probably excreted in the form of urea, uric acid or allied bodies. Notice that some of the decompositions are effected through oxidation and some through hydrolysis. But bilirubin and biliverdin are normally excreted by the liver. How do the products of the first steps in the decomposition make their way from the spleen to the liver? It has been demonstrated by Socin and many others that blood plasma which is free from corpuscles is also free from iron. Then the hæmoglobin does not pass from the spleen to the liver dissolved in the plasma. Lymph which is free from corpuscles is free from iron. We are forced to the conclusion that hæmoglobin is carried from the spleen to the liver by *white blood corpuscles.* Many observers have seen liver leucocytes filled with minute particles of matter which, when properly treated, give a micro-chemical reaction of iron. This is confirmatory of the above conclusion.

The liver will continue to secrete bile, and as a part of the bile bilirubin and biliverdin, after the spleen is extirpated. It is evident, then, that the spleen is not the only place where the first steps of red blood corpuscle katabolism may occur. Possibly it occurs *normally* in the spleen and is taken up vicariously by liver or red bone marrow after the extirpation of the spleen. Most important to note is the fact that *iron, which is the most difficult of metals to assimilate,* is, early in the katabolic process, split off and *retained in the system.*

C. THE INCOME OF ENERGY.

The income of energy is represented by the potential chemical energy of the food absorbed. To determine the amount of energy-income it is first necessary to determine the potential energy of foodstuffs and second to determine the amount of foodstuff absorbed. The first step to take in dealing with either matter or energy is to establish units by which these entities may be measured. The caloric is that amount of heat required to raise 1 gramme of water 1° C. The large calorie or kilogramme-calorie is that amount of heat required to raise 1 kilogramme of water 1° C. One kilogramme-calorie would raise 500 grammes of water 2° C., or 100 grammes 10° C.

Specific heat is the amount of heat required to raise the temperature of a given body 1° C. Water being the standard, the specific heat of the animal body is 0.8.

Quantity of heat in a body = Wt. × Sp. H. × t., *e. g.*, of a 10-kilo., dog at 38° C. = 10 × 0.8 × 38 = 30.4 kilogramme-calories.

Calorimetry is a term applied to the determination of heat units or calories dissipated by any body. The determination is made through the agency of the calorimeter.

The *calorimeter* has undergone many variations since first devised by Lavoisier and La Place in 1780. The first calorimeter, —the ice calorimeter,—was arranged with a double jacket of ice. The body whose heat radiation was to be determined was placed in a cage within the inner ice jacket. The amount of ice melted by the radiated heat gave an index of the amount of heat given off.

The *water* calorimeter of Crawford (1788) was similarly arranged except that the heat was received by a water jacket and the rise in temperature of the water indicated the amount of heat given off.

The *air calorimeter,* first used by Scharling (1849) has been found more reliable than either of the earlier forms. In its best form as used by Haldane, White and Washburn (*British Med. Journ.*, Lond., 1897, Vol. II., p. 11, cited by Schaefer) it consists of an animal chamber or combustion chamber (1) and a control chamber (Fig. 199). The body whose heat is to be determined is put into cage 1. In the control cage (2) hydrogen is burned in quantity sufficient to keep the mercury manometer balanced. The number of c.c. of hydrogen burned in an experiment is observed. The calories (gramme-calories) produced by one c.c. of hydrogen is known. Thus the gramme-calories given off by the body to be tested becomes known. Through the aid of the calorimeter one may determine not only the heat given off by the combustion of any oxidizable material—(carbon, hydrogen, alcohol, fat, starch, albumin, etc.), but also the amount radiated or conducted away from any body, *e. g.*, a living animal. With the means at hand to determine the potential energy of foodstuffs and the liberated and expended energy resulting from the katabolism of the food it is possible to test the law of the *conservation* of *energy* as applied to the animal organism and to ascertain whether or not it may be verified, in living organisms as in the realm of physical science. The first step to be taken is the determination of the potential energy of the different classes of foodstuffs.

FIG. 199.

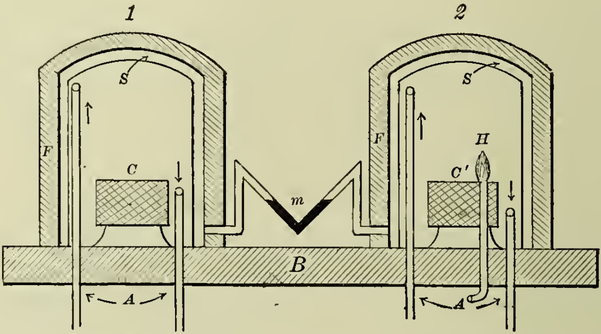


Diagram of air calorimeter. *B*, base; *F*, layer of felt; *C*, cage; *A*, ventilation tubes; *S*, air-space; *M*, mercury manometer; *H*, hydrogen flame. (After HALDANE, WHITE and WASHBURN.)

1. THE POTENTIAL ENERGY REPRESENTED BY FOODSTUFFS.

It is customary to use one heat equivalent for carbohydrates, one for proteids, and one for fats. The value used is an assumed one. The following table gives the calories represented in different foods and other substances involved in nutrition:

Substance (1 gm. dry).	Heat of Combustion	Substance (1 gm. dry).	Heat of Combustion
Starch or Glycogen	4.182 calories	Egg white 4896	5678 Calories
Cane sugar	4.176 "	" yoke 6460	
Dextrose	3940 "	Lean beef	5656 "
Lactose	4162 "	Casein	5849 "
Carbohydrates	**4181** "	Vegetable proteids	5500 "
		Proteids	*5650* "
		Urea	2523 "
Fat	9686 "	Proteid unavailable energy	1650 "
Fat	9423 "	**Proteid** available energy	**4000**
Butter	7264 "	Carbon per gramme	8080
Fats	**9400** "	Hydrogen per gramme	34662

Note that the value assumed for carbohydrates is not an arithmetical average, though it approximates an average. In computing the energy represented by a particular menu, one deals with several carbohydrates in various proportions. Instead of computing the different carbohydrates separately, it is customary to assume a convenient factor which is an approximate average, and to multiply the amount of all carbohydrates by that factor. The other foodstuffs are treated similarly.

2. THE POTENTIAL ENERGY OF COMMON FOODS.

To determine the energy which any food represents it is only necessary to find by analysis the amount of proteid, of fat and of carbohydrate which the food contains, and to multiply these amounts by the factors given in the table of energy of foodstuffs. For example: Oatmeal contains 7.6 per cent. of H_2O; 15.1 per cent. proteid; 7.1 per cent. fat; 68.2 per cent. carbohydrate, and 2 per cent. salts. One hundred grammes of oatmeal represent in energy:

From proteid . . . . . 15.1 × 4000 cal. = 60400
From fat . . . . 7.1 × 9400 " = 66740
From carbohydrate, 68.2 × 4180 " = 285076

Total . . . . 412216 calories

The energy of one pound of oatmeal is gotten by multiplying this by 4.5. The following table gives the energy value of a few common foods.

Food (market condition).	Calories per 100 gms.	Calories per pound.
Wheat Bread	286,304	1,301,241
Oatmeal	412,216	1,873,709
Cornmeal	367,428	1,670,866
Beans or Peas	358,656	1,630,091
Potatoes	84,162	382,516
Milk	56,944	258,810 [pt. 291,000]
Eggs	146,736 (2 eggs)	666,915 [doz. 880,416]
Beef	114,900	522,220
Bacon	434,400	1,974,348

3. THE ENERGY REPRESENTED BY A TYPICAL MENU.

a. An Ideal Ration for an Average Man at Light Work.

The ration given in the following table was arranged by Mrs. E. H. Richards, and is given by Thompson in his practical dietetics.

Materials.	Amount.		Proteid.		Fat.		Carbohydrate.		Calories.
	Gms.	Oz.	Gms.	Oz.	Gms.	Oz.	Gms.	Oz.	
Bread	453.6	16	31.75	1.12	2.26	0.08	257.28	9.04	1,223,674.40
Meat	226.8	8	34.02	1.20	11.34	0.40	....	....	242,672.
Oysters	226.8	8	12.52	0.44	2.04	0.07	....	....	69,256.
Cocoa	28.3	1	6.60	0.23	7.50	0.26	9.60	0.34	137,028.
Milk	113.2	4	3.63	0.13	4.42	0.16	4.88	0.17	76,466.40
Broth	456.6	16	18.14	0.64	18.14	0.64	90.72	3.20	622,285.60
Sugar	28.3	1	....	....	....	....	27.36	0.96	114,364.80
Butter	14.17	½	0.14	....	12.27	0.50	....	....	115,898.
Totals	....	....	106.8	....	57.97	....	389.84	....	2,601,649.20

b. Rations for Average Men Under Different Conditions.

The diet should vary with the requirements of the system. The ration which is adequate for a dry goods clerk would be totally inadequate for a lumberman in the northern forests. One does light work in a warm room; the other does heavy work out of doors in the coldest weather. The ration suggested under *a* would be proper for an indoor and sedentary occupation. The following table compiled by Atwater (Quoted here from Thompson's Practical Dietetics) gives an idea of requirements under various conditions.

Conditions.	Proteids.	Fat.	Carbohydrates.	Energy in Calories.
Man at light indoor work	110	60	390	2,634,200
Man at light out-of-door work	110	100	400	3,052,000
Man at moderate " "	125	125	450	3,556,000
Man at hard " "	150	150	500	4,105,000
Man at very hard out-of-door work in winter	180	200	600	5,008,000
United States Army ration	120	161	454	3,851,000
United States Navy ration	143	184	520	4,998,000
College football team	181	292	557	5,742,000
Teamsters, marble cutters, Boston	254	363	826	7,804,000(!)
Laborers of Lombardy, Italy	82	40	362	2,192,000(!)

c. Rations varied for Sex and Age.

(COMPILED FROM THOMPSON'S PRACTICAL DIETETICS.)

Variations of Sex and Age.	Proteids.	Fats.	Carbohydrates.	Calories Energy.
Children to 1½ yrs. old	28 20–36	37 30–45	75 60–90	767,000
Children 1½ to 6 yrs. old	55 36–70	40 35–48	200 90–250	1,418,000
Children 6 to 15 yrs. old	75 70–80	43 37–50	325 250–400	2,041,000
Women with light exercise (Atwater)	80	80	300	2,300,000
Women of moderate work (Voit)	92	44	400	2,426,000
Aged women	80	50	260	1,859,000
Aged men	100	68	350	2,477,000
Sewing girl, London, 93c. per week	53	33	316	1,820,000
Factory girl, Leipzig, $1.21 per week.	52	53	301	1,940,000

d. To Arrange a Menu for Particular Conditions.

If, for example, one wishes to arrange a winter diet for a student whose age is twenty-four years, weight 70 kilogrammes, who is warmly clad and who takes a moderate amount of light exercise in the open air, he would choose a diet which represents about 3,000,000 calories of energy. If the subject does not crave fat the carbohydrates must predominate as energy producers. Take, say, proteids 125 grammes, fat 90 grammes, and carbohydrates sufficient to bring the calories to 3,000,000, *i. e.*, carbohydrates 395.7. With the help of such tables of food analyses as are given above under foodstuffs (p. 283 *et seq.*) one can choose a variety and still keep the several foodstuffs approximately as suggested.

e. The Isodynamic Equivalents of Foodstuffs.

In making up dietaries one must frequently take into account the fact that fat may replace carbohydrates or *vice versa*, and that proteid may replace either. This interrelation of the foods in nutrition necessitates the use of certain coefficients called isodynamic equivalents.

The isodynamic equivalent may be expressed thus :

(I) Of proteid to fat : $\partial \left(\frac{p}{f}\right) = \frac{4000}{9400} = 0.4255.$

(II) Of proteid to carbohydrate : $\partial \left(\frac{p}{c}\right) = \frac{4000}{4180} = 0.957.$

(III) Of carbohydrate to fat : $\partial \left(\frac{c}{f}\right) = \frac{4180}{9400} = 0.445.$

With the aid of these coefficients one may readily compute the amount of one food to be substituted for another when a change of proportion is indicated. Suppose one wishes to modify the "light work menu" given above by substituting fats for the carbohydrates in excess of 350 grammes, $389.84 - 350 = 39.84$ grammes. How much fat is equivalent to 39.84 grammes carbohydrates? $\partial \left(\frac{c}{f}\right) = 0.445.$ $39.84 \times 0.445 = 17.73$ grammes of fat; $57.97 + 17.73 = 75.7$ grammes fat. The modified "light work menu" now consists of: proteids 106.8, fat 75.7, carbohydrates 350, *but it represents the same energy as before;* it is isodynamic with the menu as tabulated. It may be said here that the proteid should never fall below 100 grammes per day for an adult man or 80 grammes per day for an adult woman.

D. THE LIBERATION OF ENERGY.

a. The Primary Liberation of the Potential Energy of the Organism.

The potential chemical energy of the tissues and fluids of the body represents the capital of the organism. But this energy must be liberated—must be made kinetic—in order to figure in the life processes of the organism. In the calorimeter the energy of the foodstuffs is liberated by a process of rapid oxidation or combustion. In the animal organism the energy is liberated by a process of slow oxidation usually associated with step-by-step katabolism. It has been demonstrated that the heat is produced in the same aggregate quantity, whether the katabolism or oxidation be slow or rapid. The heat energy determined by the calorimeter, then, will be actually liberated in the organism; and if a man has a daily energy-income of 3,000,000 calories and is in a condition of material equilibrium, 3,000,000 calories of energy must be daily liberated and expended.

If the question arises: By what process or processes is the energy liberated? the answer is briefly: The processes of katabolism are the processes of energy liberation. The two processes are inseparable because in a sense identical.

In what form and in what location is the energy liberated?

It has been intimated that all of the energy is liberated in two general forms and in three locations: (I) In the form of heat and mechanical motion in the muscles; (II) as heat in the active glands; (III) as heat and something analogous to electricity,—nervous energy,—in the central nervous system and that the proportions of the total energy liberated in the several locations respectively are approximately as 16:3:1 or 80% : 15% : 5%.

b. The Transformation of Energy.

Much of the energy liberated as energy of motion is converted into heat before leaving the body. This transformation occurs by virtue of friction of the tissue and fluids. As an extreme example let us take the energy of the systole of the heart which will sum up to a prodigious amount during 24 hours. The immense sum of energy is all liberated as energy of motion, but all except an infinitesimal amount is transformed by friction of blood on walls of vessels to heat and leaves the body in that form. If the work done by the heart of the adult at each contraction is 320 grammeters, and if the heart beat about 72 times per minute then the work of the heart would amount to 77,970 calories in 24 hours (425.5 grammeters = 1 gramme-calorie) or about $\frac{1}{38}$ of the total energy usually expended, or about $\frac{5}{83}$ of a heavy day's work. Nervous energy is also transformed to heat energy.

c. The Conservation of Energy.

The law of the conservation of energy holds as absolute sway in the animal organism as in the non-living world about us. Every calorie of energy taken in either remains as stored up potential energy or it escapes from the body in the form of heat, of mechanical motion, or as in case of urea, as unliberated potential energy. The unliberated energy is, however, corrected for in the above and subsequent calculations. Rubner (*Zeitsch. f. Biol. München*, 1894, XXX., S. 73) has been successful in practically demonstrating that in the animal body the law of the conservation of energy holds good. The subject of his experiment was a 12-kilogramme dog which was confined in a calorimeter cage, thus confining the energy liberated to heat energy. The dog received during the period 228.06 grammes of proteid and 340.4 grammes of fat. This food represented a total of 4,111,970 calories. The amount of heat actually given off during this period, as shown by the calorimeter was 3,958,000 calories. Thus 96 per cent. of the energy received as potential energy of food appeared as kinetic heat energy. The remaining 4 per cent. may represent the mechanical energy of the movements made in eating the food or other movements made even in a confined space. In another experiment the net energy received in the ingesta 278,500 calories; the heat energy given off 276,800; in this case over 99.3 per cent. of the energy was given off as heat leaving less than 0.7 per cent. for mechanical energy.

d. The Expenditure of the Kinetic Energy of the Organism.

All of the kinetic energy of the body is finally expended in one or the other of two forms: *as heat; or as motion.* A certain amount of energy which enters the system as potential energy leaves as potential energy. The matter holding this energy is urea, uric acid, fæces, milk, the reproductive products and the oil secreted by the skin, or other epidermal products which are shed, moulted or abraded.

We are now in a position to take an exact account of the income and expenditure of the energy of the organism and may express the fact that the two amounts are equal through the use of a *Balance Sheet.*

BALANCE SHEET OF ENERGY FOR MAN AT LIGHT WORK.

	Income in Calories.	Expenditure in Calories.
INCOME :—		
Proteids : 110 grammes @ 4000 calories	440,000	
Fats : 100 grammes @ 9400 calories	940,000	
Carbohydrates : 400 grammes @ 4180 calories	1,672,000	
EXPENDITURE :—		
Mechanical work, 212, 750 kilogrammeters		500,000
[425.5 grammeters equivalent to calorie]		
Heat lost in 1900 grammes of excreta		47,500
[Cooling from 37°C. to 12°C. : 1900×25 calories]		
Heat required to warm 13000 grammes air from 12°C. to 37°C.		84,500
[Specific heat of air = 0.26, ∴ 13000 × 25 × .26]		
Evaporating 330 grammes of water from lungs		192,600
[1 gramme requires 582 calories]		
Evaporating 660 grammes of water from skin		384,120
Radiation and conduction from skin about		1,843,820
	3,052,000	3,052,000

With varying muscular activity and varying external temperature there will be a fluctuation of the credit side of the account. If the balance is against the system the reserved nutrients are called out for an immediate adjustment of the account. Later the reserve is made good by a more liberal diet.

E. ANIMAL HEAT.

a. General Considerations.

The subject of animal heat belongs logically under *Liberation of Energy.* Many of the things usually discussed under animal heat have already been treated above. The very great importance of certain phases of this subject justifies especial emphasis under a separate heading.

From what has preceded it goes without saying that the heat of the animal body is the liberated heat of metabolism. This heat is subject to constant additions through metabolic activity of the tissues and to constant subtractions through radiation or conduction from the surface.

One of the most remarkable mechanisms in the animal body is the heat-regulating apparatus. Through its operation certain animals are able to maintain a fairly constant temperature whatever the temperature of their surrounding medium may be. Animals thus able to maintain an even temperature in an uneven medium are called *Homoiotherms;* (*ὅμοιος*—like) while animals which are not able to maintain an even temperature, but whose temperature varies with that of the surroundings are called Poikilotherms (*ποικιλος*—varied). Poikilothermal or "cold-blooded" animals, by virtue of their sluggish metabolism, have a temperature somewhat higher than the medium when the latter has a relatively low temperature; but above a certain point the temperature of the animal falls somewhat below that of the medium. This is well illustrated by the frog. The frog's temperature in water at 2.8° C. is 5.3° C., in water at 20.6° C. is 20.7° C. and in water at 41° C. is 38° C. The poikilothermal animals are the reptiles, amphibia, fishes, and invertebrates.

The homoiothermal or "warm-blooded" animals include the birds and mammals. The following mean temperatures per rectum have been determined: Horse, 37.9°C.; cow, 38.6°C.; sheep, 40.2°C.; dog, 38.6°C.; cat, 38.7°C.; pig, 38.7°C.; rabbit, 39.2°C.; guinea-pig, 38.7°C.; white rat, 38°C.; monkey, 38.4°C.; common fowl, 41.6°C.; duck, 42.1°C.; pigeon, 40.9°C.; whale, 38.8°C.; seal, 38.9°C.; great titmouse (a bird), 44°C., (111°F.); yellow hammer, 43.2°C.

b. Method of Determining the Mean Temperature.

The usual method of determining the temperature of an animal is to insert a mercury thermometer into some inclosed space, holding it in position until the thermometer registers. Various locations are chosen: the mouth, the axilla, the groin, the rectum, and the vagina. The location most usually chosen—the mouth—is the one which is subject to the greatest accidental variations. Observation has shown that the most reliable and unvarying temperature may be gotten by inserting the thermometer several centimeters (3–6 cm.) into the rectum or vagina.

The thermometer should register tenths of a degree. The temperatures recorded above are in the Centigrade scale, in which the difference in the stand of the mercury column at freezing and at boiling is divided into 100 parts or *degrees Centigrade*. The Fahrenheit scale, most used in America, differs from the Centigrade in arbitrarily assuming for the freezing point +32° and for the boiling point +212°, dividing the space between these two points into 180° F., 1° F. is equal to $\frac{5}{9}$°C., or 0.5°C.; while 1°C.=1.8° F. To reduce a centigrade reading to Fahrenheit it is only necessary to multiply by 1.8 and add 32°; *i. e.*, 38°C.=[38 × 1.8+32] 100.4° F.

To reduce a Fahrenheit reading to Centigrade one subtracts 32° and multiplies by 0.5, thus 100.4°F. (100.4 − 32° = 68.4 × .5) = 38°C.

From what will follow it will be evident that in the collection of data for comparison uniformity of method must be observed throughout a series of observations. If one wishes to determine the mean rectal temperature in the human subject he should make the observations at a particular time in the day, otherwise his results will be varied by two factors. If he wishes to compare oral with rectal temperature he should observe as indicated above, every precaution to eliminate every other variable except the one whose value he wishes to determine. If he attempts to compare the early morning temperature of a man with the evening oral temperature of a child his results will be valueless.

c. Factors Which Cause Variations of Temperature.

1. **Climate.**—There is very little difference in the body-temperature of the races inhabiting frigid, temperate and torrid zones; but if a native of the frigid zone travels into the torrid zone his temperature will rise several tenths of a degree higher than the normal for the reason that his organs of heat regulation can not easily adjust themselves to so profound a change in the environment, and the heat accumulates in the body. When, on the other hand, a native of the torrid zone is subjected to a frigid temperature, his heat production cannot keep pace with the heat expenditure and his temperature falls slightly below the normal.

2. **Sex.**—Sex exerts little influence. Extended observations have determined that the temperature of a bitch is 0.2°C. lower than that of a dog; that the temperature of a female duck is 0.3° C. higher than that of the male duck; that the temperature of the mare is 0.4°C. higher than that of the stallion. This difference is small and inconsistent. The results for the human subject are contradictory, but the temperature of the woman seems to be slightly higher than that of the man.

3. **Age.**—Infants and children have a mean temperature higher than the mean temperature of the adult by about 0.4° C. After puberty the temperature reaches the level of the adult temperature, which level it maintains throughout life with possibly a slight rise in rectal temperature with old age.

4. **The Changing Season.**—The oral temperature follows the seasons, being slightly higher in summer and slightly lower in winter. The rectal temperature is higher in the winter and early spring than at any other time during the year. (Bosanquet, *Lancet*, London, 1895, Vol. I., p. 672.)

Animals have a remarkable resistance to the extremes of climatic changes, the body temperature not rising perceptibly when the external rises several degrees Centigrade above the temperature of the blood. On the other hand animals and men subjected to sudden fall of temperature in winter will maintain an equable temperature.

5. **Extreme Temperatures Artificially Produced.**—When an animal is subjected to extreme heat much in excess of that which it may experience with the changing seasons it is able to maintain a fairly even temperature for some time *if the heated air be dry*, while in moist heat the temperature quickly rises and

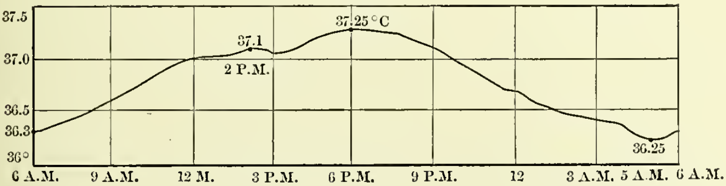
death ensues. The reason for this is simple: in dry air the evaporation from the surface keeps the temperature down; while in moist air the evaporation is reduced or quite suspended and the animal has no defense against the extreme high temperature.

When a homoiothermal animal is subjected to extreme cold the protective process consists in retaining enough of the liberated heat to keep the temperature up to normal. The coat of hair or feathers or subcutaneous fat usually suffices in all animals which are accustomed by nature to low temperature. Animals not so protected succumb soon.

Cold-blooded animals, especially fish, may be cooled to so low a temperature, — 1° C. to — 3° C., that there is a torpor simulating death; but with gradual rise of temperature the life processes start up again.

6. **The Influence of Day and Night.**—The following chart gives the result of observations by Jürgensen and Liebmeister (*Handbuch der Pathologie und Therapie des Fiebers*, Leipzig, 1875). Note that the lowest temperature is at 5:00 A. M., and the highest from 5:00 P. M. to 7:00 P. M. The range is just 1° C. or 1.8° F.

FIG. 200.



Daily variation of temperature. (After JÜRGENSEN.)

The cause for these variations seems to be the bodily activity of the day and the rest of the night because in men who work nights and sleep during the day the curve is practically reversed.

7. **Muscular Work.**—The muscles are the heat-producing organs *par excellence*, 80 per cent. of the heat energy of the body being liberated in the muscles. The heat-producing function of the muscles is not by any means independent of their contractility. Just how far these two functions are interdependent is undetermined. It is certain that when an urgent call for more heat is made upon the system the muscles respond with involuntary jerky contractions (*shivering*). The natural impulse is for the animal to begin active voluntary exercise to "warm up." On the other hand, heat is produced in the muscles when they are apparently at perfect rest so far as any visible or sensible contractions are concerned; yet if the muscles are paralyzed by curare they lose their heat-producing power and the animal is at

the mercy of external temperature, *i. e.*, potentially a "cold-blooded" animal. There is an increased production of heat during exercise; if the increased amount of heat is not given off from the body as fast as it is liberated within the body there will be a rise of temperature. Repeated observations by numerous observers show that vigorous muscular exercise may be attended by a rise of as much as 1.2° C.

8. **Mental Work.**—For reasons similar to those cited above under *muscular work*, there is a rise of temperature accompanying vigorous mental work. This rise is local and may or may not be communicated in perceptible degree to the system in general, though it is usually conceded that the general temperature may rise as much as 0.7° C. with mental work.

9. **Food.**—The increased activity of the digestive glands, and of the involuntary muscles of the digestive system causes a somewhat increased production of heat. At the same time a large proportion of blood is collected in the central organ—less upon the surface—and the heat expenditure is decreased. These two things, working together, tend to raise the temperature. When other factors tend to lower the temperature a meal would have the effect of keeping up the temperature when it would otherwise fall. This is the effect of a dinner at night.

10. **Sleep.**—Sleep in itself has no influence directly upon temperature. Perfect rest which accompanies sleep causes a slower production of heat and consequently a fall of temperature.

11. **Baths.**—When a warm-blooded animal is immersed in a bath it is at the mercy of two factors: heat-production and heat-conduction. The first factor is not likely to differ much from the normal, so that the principal factor is the temperature of the bath. If it is above blood temperature the body-temperature will rise. If the temperature of the bath is below that of the blood,—the usual condition,—the temperature will tend to fall, though it must be remembered that the heat-producing factor may in this case be an important one. If the temperature of the bath is much below that of the blood the fall of body temperature may be considerable. A 12-minute bath in sea water at 6.7° C. caused a fall of oral temperature from 36.7° C. to 34° C.

12. **Drugs.**—*Alcohol,* by increasing cutaneous circulation, causes a fall of temperature.

Chloroform, ether, morphine, chloral, and *nicotine* cause a fall of temperature through decreased heat production.

Curari causes fall through paralysis of the muscles followed by decreased heat production.

Cocain, atropin, caffein, and *veratrin* raise the temperature through decreased heat radiation or increased heat production.

13. **Individual Differences of Temperature.**—The mean

temperature of individuals of the same species living under exactly the same circumstances will not always be the same. The mean temperature of one man may differ by as much as 0.7°C. from that of another, all conditions being apparently the same.

14. **The Limits of the Variations.**—Pembrey gives the maximum range of normal human temperature as 2° C. (3.6° F.). "By exposure to cold, especially when subjects are drunk, the temperature may fall as low as 24° C. without a fatal issue." (Pembrey-Schaefer's Text-book of Physiology, Vol. I., p. 821.)

The maximum temperature compatible with life as reported by Wunderlich is 44.75°C. (112.6°F.). Death followed.

d. Temperature Topography.

(*a*) Temperature in Superficial Cavities:
  (I) Bend of knee = 35°C.
  (II) Inguinal fold = 35.8°C.
  (III) Closed axilla = 36.5°C.
  (IV) Mouth (under tongue) = 37.2°C.
  (V) Rectum = 38°C.
  (VI) Vagina = 38.3°C.
(*b*) Temperature of Fluids and Tissues:
  (I) Blood in left heart = 38.8°C.
  (II) Blood in right heart = 38.8°C.
  (III) Blood in hepatic vein = 39.7°C.
  (IV) Blood in crural vein = 37.2°C.

e. Heat Regulation or Thermotaxis.

1. **Relation of Heat-Generation to Heat-Expenditure.**—In order to maintain an even temperature of body in a medium of widely varying temperature it is necessary that the organism be provided with some means of adjusting either the rate of heat production or the rate of heat radiation. The factors which work together to maintain the *thermotactic condition* are called *thermogenetic* and *thermolytic* factors. These two factors have the following relation to Thermotaxis; the greater the thermogenesis the higher the temperature; the greater the thermolysis the lower the temperature. If we represent the temperature which is produced in the body by the interaction of these factors by t, the thermogenetic factor by g, and the thermolytic factor by l then:

$$t = \frac{g}{l}$$

(*a*) Variation of One Factor.—From the above expression it is evident that the temperature will be increased (raised) by an increase of g, $\left(t = \frac{mg}{l}\right)$ or by a decrease of l $\left(t = \frac{g}{\frac{1}{n}l}\right)$. In verbal expression :—*the temperature will be raised by an increase of heat-formation or by a decrease of heat-radiation.*

Furthermore, *the temperature may be lowered by a decrease of heat-formation* $\left(t = \frac{\frac{1}{m}g}{l}\right)$, *or by an increase of heat-radiation,* $\left(t = \frac{g}{nl}\right)$.

(*b*) VARIATION OF BOTH FACTORS TOGETHER.—Both of these factors may increase at the same time. The situation may be expressed mathematically as follows : . . . . $t = \frac{mg}{nl}$.

If $m = n$; *i. e., if both are increased proportionally there will be no change in the temperature* for the expression reduces at once to the normal, $t = \frac{g}{l}$. If $m > n$; *i. e., if heat-formation increases more than heat-liberation the temperature will rise.* If $m < n$; *i. e., if the heat-liberation increases more than the heat-formation there will be a fall of temperature.*

But the thermotactic factors may both decrease at the same time ; expressed mathematically as follows :. . . . $t = \frac{\frac{1}{m}g}{\frac{1}{n}l}$.

If $\frac{1}{m} = \frac{1}{n}$; *i. e., if heat-generation is decreased proportionally with heat-radiation the temperature would remain unchanged.* If $m > n$; *i. e., if heat-generation is decreased more than is heat-radiation there would be a decrease* (*fall*) *in temperature.* If $m < n$; *i. e., if heat-generation is decreased less rapidly than is heat-liberation there would be an increase* (*rise*) *in temperature.*

2. **Thermotactic Centers.**—(*a*) THERMOGENETIC CENTERS : (I) On median side of corpus striatum ; (II) between corpus striatum and optic thalmus ; (III) in anterior end of optic thalmus.

Thermogenetic centers may be : *Thermoaugmentor or Thermoinhibitory* and the thermogenetic impulses pass from the centers to the metabolic tissues along the trophic nerves supplying those tissues.

(*b*) THERMOLYTIC CENTERS.—The factors of thermolysis are : (I) radiation ; (II) evaporation.

Both radiation and evaporation must take place from the surface of the skin or respiratory mucous membranes, principally the former.

Dilatation of the cutaneous arterioles favors both radiation and increased secretion of perspiration. Contraction of the arterioles has the reverse influence upon radiation and evaporation. It then becomes evident that both factors of thermolysis may be increased by vaso-cutaneous dilatation. The vaso-motor centers may be classified as (α) vaso-constrictor and (β) vaso-dilator.

(α) The *vaso-constrictor center* is bilateral and is located in the anterior end of the floor of the fourth ventricle. This center is always in action and constant impulses from it to the various vessels causes their *tonus*. This center seems to be general in its jurisdiction and various stimuli may, through its action, cause *general* increase or decrease of vaso-constriction accompanied by general rise or fall of blood-pressure.

(β) *The vaso-dilator centers* are not centralized in some circumscribed part of the brain or cord, but "diffuse," *i. e.*, small local centers are located intra- and extra-cranially along the central nervous axis. The purpose of this becomes evident when we remember that these centers *act locally*, their apparent function being *to increase local blood* supply.

"There is in some degree an inverse relation between the vessels of the skin and those of deeper parts on reflex stimulation of vaso-motor centers. The cutaneous vessels are often dilated while those of the deeper parts are constricted." (Am. Text-book, quoting from Franck, p. 502, 1896.) This fact makes it evident that the whole surface of the skin may flush through vaso-dilatation, but the blood-pressure still kept up by vaso-constriction in the deep-lying tissues.

Evaporation is increased or decreased through the influence of ,—(.γ) *the sweat-center*, which is bilateral and located in the medulla.

All of these centers are stimulated reflexly by the temperature of the medium which comes in contact with the skin. If cold, then the thermogenetic center is stimulated and the metabolic tissues begin a more active katabolism. Meanwhile the heat supply is conserved by a withdrawal of the blood from the periphery, *i. e.*, vaso-contrictor center stimulated. Presently the heat accumulates through conservation and production, and a reaction sets in expressed by a cutaneous vaso-dilatation. The blood comes to the surface, warms the skin, and by exposure falls in temperature to the normal.

On the other hand, when the medium is too hot, the sensory nerves in the skin carry impulses to the centers: (I) the thermogenetic activity is inhibited; (II) the sweat-center is stimulated, the perspiration pours out upon the skin and its evaporation cools the body. The interaction of the controlling factors keeps the temperature within about one-half degree of the average, *i. e.*, within a range of about one degree, though under less usual circumstances 2°C.

Various causes may operate to bring about an abnormally high or low temperature, especially the former. This condition which is a pathological one is a symptom incident to many diseases and will be treated in full under Pathology.

CHAPTER VIII.

EXCRETION.

INTRODUCTION.

1. DEFINITIONS.
2. GENERAL CONSIDERATIONS.
3. ANATOMY OF THE KIDNEY.
    - *a.* Blood Supply of the Kidney.
    - *b.* The Uriniferous Tubules.
    - *c.* The Innervation of the Kidney.

THE PHYSIOLOGY OF EXCRETION.

A. RENAL EXCRETION.

1. THE URINE.
    - *a.* General Characters.
        - (1) *Quantity.*
        - (2) *Specific Gravity.*
        - (3) *Reaction.*
        - (4) *Color.*
    - *b.* Chemical Composition. Tabulated.
    - *c.* The Urinary Constituents Separately Considered.
        - (1) *Organic Constituents.*
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2. THE PROCESS OF URINARY EXCRETION.
    - *a.* Glomerular Excretion.
        - (1) *Experiments and Conclusions from same.*
        - (2) *Factors Influencing Glomerular Excretion.*
    - *b.* Glandular Excretion.
    - *c.* The Egestion of Urine. Micturition.

B. PULMONARY EXCRETION.

C. CUTANEOUS EXCRETION.

1. THE SWEAT.
    - *a.* General Characters.
        - (*a*) *Quantity;* (*b*) *Specific Gravity;* (*c*) *Reaction.*
    - *b.* Chemical Composition.
        - (1) *Organic Constituents.*
        - (2) *Inorganic Constituents.*
2. THE PROCESS OF CUTANEOUS EXCRETION: PERSPIRATION.
    - (1) The Influence of the Nervous System Upon Cutaneous Excretion.
    - (2) Factors Which Cause a Variation in the Quantity of Perspiration.

D. INTESTINAL EXCRETION.

EXCRETION. INTRODUCTION.

1. DEFINITIONS.

Excretion.—"The separation of waste products of an organ or of the body of a whole, out of the blood. The material so excreted" (Gould). Comparison of this definition with that of *secretion* (p. 246) shows that excretion is looked upon as a special form of secretion; the distinction being that secretion is elaboration of any product from constituents of blood or lymph while excretion is the *separation of waste products from the blood or lymph.*

Egestion.—"The expulsion of excrements or of excretion." (Gould.)

Egesta.—"(pl. of egestum, fecal matter.) The discharges of the bowels or other emunctory organs." (Gould.) Let us make a specific application of these definitions. The parietal cells of the gastric glands take up NaCl and H_2CO_3, or $CaCl_2$ and Na_2HPO_4 from the blood, where they form normal constituents; and these active cells *elaborate new products.*

An excretion differs from a typical secretion in that the former represents waste products which escape, from the place where the katabolism occurred, into the lymph or blood and so circulate through the system until brought to some organ whose active cells have the power to *select* and *separate these waste products out of the blood.* For example, urea is secreted (internal secretion) by the liver, but excreted by the cells of the convoluted tubules of the kidney.

The term egestion is a general one and includes all of those acts which have as their end the *throwing out of excretions especially,* though the term may, not improperly, be used to include not only the throwing out of the excreta, but also of matter which has never formed a part of the body, *e. g.,* the undigested portion of food; and also the unabsorbed part of the inspired air—the nitrogen.

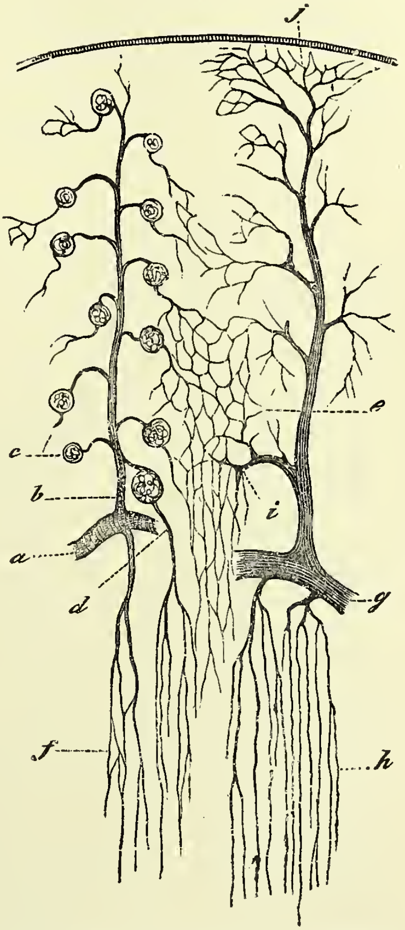
Egestion, then, is represented by the following special acts; (1) Defecation, (2) Micturition, (3) Perspiration, (4) Expiration. The matter thrown out of the organisms by these acts may be called, collectively, EGESTA; while the term EXCRETA may be used only for *that part of the egesta* which was at one time a constituent of the body and has been reduced to a condition useless to the organism and has been excreted by the lungs, the skin, the kidneys or the liver.

2. GENERAL CONSIDERATIONS.

We have now followed the process of nutrition to its last stage,—ridding the body of the waste products. We have studied the process and products of digestion and have enumerated the factors involved in the absorption of digested foods; we have studied examples of the anabolic changes which occur during the assimilation of the absorbed matter, and of the katabolic changes which occur incident to the activity of the tissues. We have noted from time to time the formation of some body useless to the animal organism. Frequently, indeed, these bodies are worse than useless,—they may be poisonous. In either case it is necessary that the organism be provided with some means of throwing off the useless or poisonous matter. But what is the character of this waste matter as we have, up to this point, noted it? 1st. There was a gas—CO_2—the product of the oxidation of the tissues. 2d. There was water, in part the unchanged water of imbibition, in part the product of oxidation of the hydrogen of the tissues. 3d. There was solid material composed of: (I) certain organic bodies—urea, hippuric acid; (II) inorganic salts—$NaCl$, $HKSO_4$, etc. If one were to compare this list of material "*outgo*" with the list of material "*income*"—the foods—one would note a remarkable parallelism in the general character of the matter, *i. e.*, both lists contain a gas, water, and solids composed of organic and inorganic matter, the organic matter containing nitrogenous and non-nitrogenous bodies and the inorganic matter containing a long list of chlorides, phosphates, and sulphates. But the parallelism vanishes as soon as one glances at the *specific* character of the "income" and "outgo" matter: the "income" represents matter of high potentiality, while the "outgo" represents matter completely, or almost completely, depleted of its energy. The method of liberation and expenditure of this energy has been discussed.

The only situations where the waste products could be thrown out of the system are the boundary surfaces. These boundary surfaces include the skin and all of the mucous surfaces, including the genito-urinary epithelium. Of all these possible situations certain locations are specialized for typical secretion only (*e. g.*, genital, conjunctival epithelium), certain locations are specialized for absorption only (villi of small intestines); certain locations are devoted in part to secretion and in part to absorption (epithelium of stomach and large intestine). The only portion of the boundary epithelium which is specialized exclusively for excretion is the *renal epithelium*. The pulmonary epithelium is nearly as much devoted to absorption as to excretion. The general cutaneous surface is, first of all, an organ of protection, secondarily, an organ of thermolysis where the water secreted by the sweat glands serves a specific purpose. Quite subordinate to the two functions mentioned above, the skin is an organ of excretion supplementing the work of the kidneys in the excretion of water.

FIG. 201.



Vascular supply of kidney. (CADIAT.) Diagrammatic. *a*, part of arterial arch; *b*, interlobular artery; *c*, glomerulus; *d*, efferent vessel passing to medulla as false arteria recta; *e*, capillaries of cortex; *f*, capillaries of medulla; *g*, venous arch; *h*, straight veins of medulla; *j*, vena stellula; *i*, interlobular vein. (SCHAEFER.)

Of the epithelium lining the alimentary canal it can not be said that it is excretory in any sense. A portion of the secretion (mucus, etc.), passes out of the canal with the fæces, but it is secreted for a particular local function and is not separated out of the blood to rid the system of it. The hepatic epithelium, however, forms several excreta, among which are urea, which is excreted by the kidney, and bile pigments which are excreted by the liver itself.

To summarize: excretion takes place at four more or less specialized parts of the boundary epithelium: (I) *the renal epithelium*, (II) *the pulmonary epithelium*, (III) *the general cutaneous surface*, (IV) *the hepatic epithelium*.

The physiologically important features of the structure of the lungs and of the liver have been summarized under respiration and metabolism. The structure of the skin will be given under the subject, External Relations. The only organ solely excretory in its function is the kidney whose anatomy may be here summarized.

3. ANATOMY OF THE KIDNEY.

The following summary presents the facts of greatest importance to the physiologist.

a. The Blood-Supply of the Kidney.

(1) The large short *renal artery* direct from the abdominal artery carries to the kidney its supply of arterial blood. Its size is wholly out of proportion to the kidney, making it evident at once that another purpose than simple nourishment of the kidney tissue is to be accomplished.

(2) The large, short *renal vein* emptying direct into the vena cava offers slight resistance to the return of the blood.

Fig. 202.

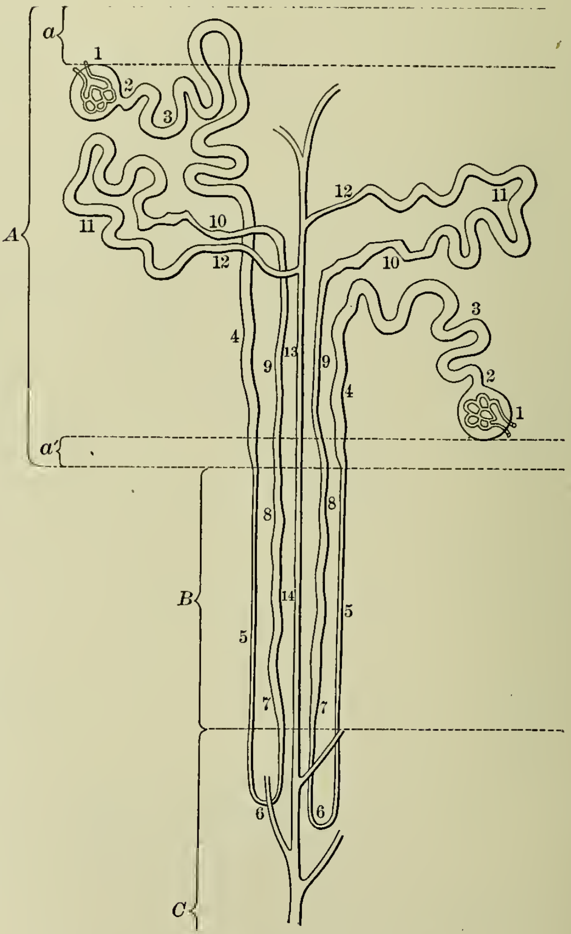


Diagram of the course of two uriniferous tubules. (Klein.)

(3) The formation of a network of arterial and venous arches between the cortex (*A*, Fig. 202) and the medulla (*B C*, Fig. 202) in and just below the plane *a′* (see *a* and *g*, Fig. 201).

(4) The *interlobular cortical arteries* passing upward from this plane. (*b*, Fig. 201.)

(5) The *glomeruli* or tufts of capillaries on either side of the interlobular arteries. (*c*, Fig. 201.) Each glomerulus is supplied by an *afferent* arteriole and is emptied by an *efferent* venule.

(6) The capillaries of the cortex (*e*, Fig. 201) surrounding in a network the tubules of the cortex and fed by the *efferent* venules.

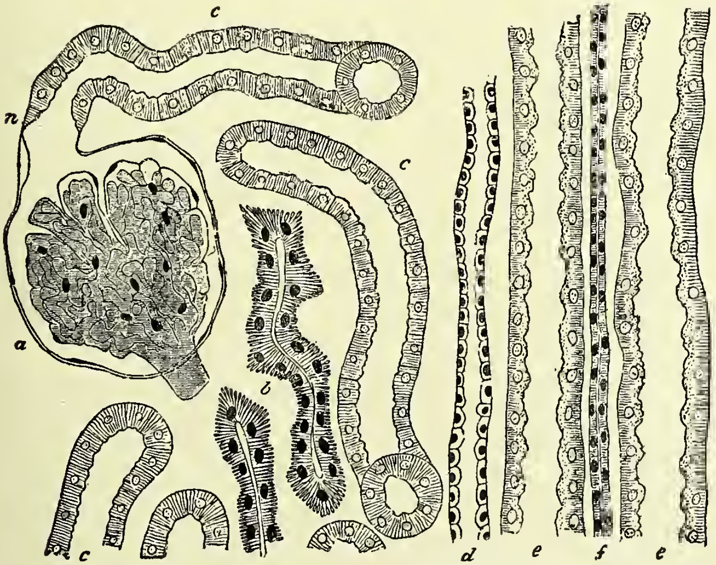
(7) The capillaries of the medulla fed by the *true* and *false arteriæ rectæ.* (*d′* and *d*, Fig. 201.)

(8) The *interlobular veins* collecting the blood from the cortex and through the *venous arches* passing it into the larger branches of the renal vein.

b. The Uriniferous Tubules.

(1) *Capsule* of Bowman inclosing a glomerulus. The glomerulus, though inclosed by the capsule, is outside of the uriniferous canal, because the capsule is reduplicated, one layer of it lying upon the glomerulus. (*a*, Fig. 203, and 1, Fig. 202.)

Fig. 203.



Tubules from a section of dog's kidney. *a*, capsule, inclosing the glomerulus; *n*, neck of the capsule; *c*, *c*, convoluted tubules; *b*, irregular tubules; *d*, collecting tube; *e*, *e*, spiral tubes; *f*, part of the ascending limb of Henle's loop, here (in the medullary ray) narrow. (Schaefer after Klein.)

(2) The *neck* of the capsule, beyond which the real tubule begins.

(3) The *proximal convoluted tubule* (3, Fig. 202, *c*, Fig. 203), clothed with striated cuboidal epithelium.

(4) *The spiral portion* (4 and *e*, Figs. 202 and 203), with low granulo-striated epithelium and wavy course.

(5) The *descending limb* of *Henle's loop* (5, Fig. 202), possessing the narrowest lumen of the entire tubule surrounded by flattened plates whose nuclei project into the lumen of the tubule.

(6) The *loop* of *Henle* and the ascending *limb* of *Henle's loop* (6, 7, 8, 9, Fig. 202; and *f*, Fig. 203) with polyhedral cells and flattened nuclei.

(7) The *irregular portion* and the distal convoluted portion (10, 11, Fig. 202); (*b* and *c*, Fig. 203) whose epithelium is similar to that of the proximal convoluted portion.

(8) The *collecting tubules* of the *medullary ray* (12, 13, Fig. 202; and *d*, Fig. 203), with cuboidal transparent epithelium.

(9) The *excretory ducts* of the *medullary portion* (14, 15, Fig. 202), whose epithelium consists of large, well-defined, columnar cells with ellipsoidal nuclei near the base.

c. **Innervation of the Kidney.**

The kidney is supplied by branches from the *renal plexus* which surrounds the renal artery. The renal plexus is, in turn, "formed by filaments from the solar plexus, the outer part of the semilunar plexus, and the aortic plexus. It is also joined by filaments from the splanchnic nerves. The nerves from these sources—fifteen or twenty in number—have numerous ganglia developed upon them. They accompany branches of the renal artery into the kidney." (Gray.)

The ultimate origin of this plexus is a center in the floor of the fourth ventricle, anterior to the vagus center. Section of the nerve-tract anywhere between the center and kidney causes increase in size of kidney and polyuria or hyduria. Stimulation of the peripheral end causes shrinking of the kidney and decrease of excretion. These experiments lead to the conclusion that the renal plexus carries principally *vaso-constrictor* fibers. Other experiments show that there are vaso-dilator fibers. The existence of a specific secretory center has not been demonstrated. That some local center must exist is indicated by the response of the excised kidney, in size and activity of excretion to certain perfused drugs.

THE PHYSIOLOGY OF EXCRETION.

A. RENAL EXCRETION.

1. THE URINE.

a. General Characteristics.

1. **The Quantity.**—An average sized man passes about 1500 c.c. in 24 hours. This amount varies from 1200 c.c. to 1700 c.c. according to various conditions, the chief factors which increase the quantity being increased imbibition and decreased perspiration. Either of these two things or both together usually accounts for increased urinary excretion.

2. **The Specific Gravity.**—The urine consists of a number of soluble solids in solution. The amount of the solids is less variable than the amount of the water but the proportion may vary considerably. The specific gravity varies between the usual normal limits 1015 and 1025. The factors enumerated above which increase the quantity, at the same time decrease the specific gravity because it is the water rather than the solids which is increased. If the limits given above are exceeded in either direction the cause should be determined. To pass beyond these limits does not by any means necessarily indicate a pathological condition. Halliburton gives as extreme physiological limits 1002, after excessive imbibition and 1035, after copious sweating. But these are unusual limits, and habits which could lead to such extreme dilution or condensation of urine might readily lead to nutritional disturbances.

3. **The Reaction.**—Normal human urine is usually acid when passed. The urine of carnivora is strongly acid; that of herbivora and vegetarians is either faintly acid or alkaline. The acidity of urine is due to the presence of acid sodium phosphate (NaH_2PO_4). In average urine about 60 per cent. of the phosphoric acid present is in the form of NaH_2PO_4. When other acids pass into the blood from the metabolic tissues or the absorptive surface they take bases from the monohydrogen phosphate and thus increase the dihydrogen phosphate, so increasing the acidity *indirectly*, the acid body in the urine being in every case *dihydrogen phosphate*, particularly NaH_2PO_4.

Bunge called attention to the fact that the secretion of HCl into the lumen of the stomach is accompanied by a quantitative (internal) secretion of bases into the circulation. This will tend to decrease the acidity of the urine, because the alkali thus liberated combines with the acids produced in other metabolic processes forming neutral salts and protecting monohydrogen phosphate from the acids in question. This accounts in part for the decreased acidity of the urine during digestion.

The reason for the alkalinity of the urine of herbivora is that their food contains a considerable quantity of alkaline bases (Na and K) in combination with organic acids (tartaric, citric, malic). These acids become oxidized in the body and the metals combine with CO_2 to make carbonates whose excretion in the urine neutralizes the acids and leaves the liquid alkaline in reaction.

To summarize : *The reaction of the urine is, in man, normally acid. The acidity is due to acid phosphates. The acidity is increased by increased proteid metabolism. The acidity is decreased by ingestion of the bases in combination with organic acids. The acidity is decreased by the secretion of HCl. The alkalinity of the blood is decreased* (acidity of urine increased) *by the secretion of bile and pancreatic juice.*

4. **The Color.**—The normal light yellow varies with the specific gravity shading into brown with increasing specific gravity and becoming almost as clear as water with decreasing specific gravity.

b. The Chemical Composition of the Urine.

The Chief Urinary Constituents.	Parkes.			Bunge.	
	Percentage Composition.	Quantities in 24 hours.	Per Diem per kilo. body weight.	Per diem on meat and water diet.	Per diem on bread, butter and water
	Grammes	Grammes	Grammes	Grammes	Grammes
Urine	100.00	1500	23.9657	1672c.c	1920c.c
Water	95.164	1427.46	22.8600	....	....
Solids	4.836	72.54	1.1057	90.607+	45.448+
(1) Organic	3.003	45.04	0.6794	?	?
(*a*) Nitrogenous	2.336	35.04+	0.5284	70.761+	21.814
(α) Urea	2.212	33.18	0.5000	67.200	20.600
(β) Kreatinin	0.060	0.91	0.0140	2.163	0.961
(γ) Uric Acid	0.037	0.55	0.0084	1.398	0.253
(δ) Hippuric Acid	0.027	0.40	0.0060	?	?
(ε) Xanthin Bodies	0.666	10.00	0.1510	?	?
(ζ) Amido-Acids					
(*b*) Aromatic Substances					
(*c*) Carbohydrates					
(*d*) Other organic bodies including Pigments					
(2) Inorganic	1.833	27.50	0.4263	19.846	13.634
(*a*) Acids	0.845	12.67	0.2045	11.928	7.919
(α) Chlorine	0.500	7.50	0.1260	3.817	4.996
(β) Phosphoric [P_2O_5]	.211	3.16	0.0480	3.437	1.658
(γ) Sulphuric [SO_3]	.134	2.01	0.0305	4.674	1.265
(*b*) Bases	0.988	14.83	0.2218	7.918	5.715
(α) Sodium	0.739	11.09	0.1661	3.991	3.923
(β) Potassium	.167	2.50	0.0420	3.308	1.314
(γ) Ammonia	.051	0.77	0.0130	.... ..	....
(δ) Calcium	.017	0.26	0.0004	0.328	0.339
(ε) Magnesium	.014	0.21	0.0003	0.291	0.139

c. The Urinary Constituents Separately Considered.

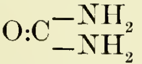
The quantity of *water* eliminated from the system by way of the kidneys is far more constant than the quantity ingested, the range of the former being about 500 c.c. (1200–1700) while the range of the latter is as much as 1000 c.c. One of the excretory organs must present a range sufficiently wide to cover that shown by the water imbibed. The skin fulfills this requirement. The relation between the quantity of water ingested and that excreted by skin and kidneys together, with the reciprocal relations between skin and kidneys will be discussed at length with the functions of the skin.

The quantity of solids excreted by the kidneys is subject to a considerable range. Note in the above table that with a meat diet the solids are about twice as great in quantity as with a bread diet; and that with a mixed diet (second column) the quantity is midway between that of the pure proteid and the vegetarian diet. By far the greater part of the solids leaves the body by the kidneys.

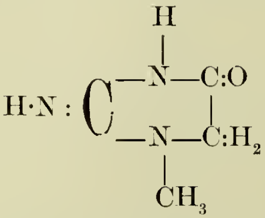
1. **Organic Compounds.**—The relation between organic and inorganic varies within rather wide limits; for a mixed diet the organic : inorganic :: 5:3; for a meat diet the organic matter is probably at least four times as great in quantity as the inorganic, while with the vegetarian diet the relations approach those of a mixed diet.

(*a*) NITROGENOUS COMPOUNDS. About 94 per cent. (15 grammes daily) of the nitrogen leaves the body through the kidneys, the remaining 6 per cent. (1 gramme daily) leaves the body in the intestinal secretions, cutaneous and pulmonary. The nitrogenous excreta are much affected by the diet. Note that with a meat diet they aggregate twice as much as with a mixed diet. Of the nitrogen of the urine about 86 per cent. is in the urea, 3 per cent. in kreatinin, 2 per cent. in uric acid and xanthine bodies, 6 per cent. in other nitrogenous compounds including hippuric acid, amido-acids, indol, skatol, pigments, and neucleo-albumin; and 3 per cent. in ammonia.

Ammonia should probably be classified with the nitrogenous compounds, but inasmuch as it appears as a base among the inorganic constituents of the urine the author has classified it as an inorganic base, under which head it will be discussed.

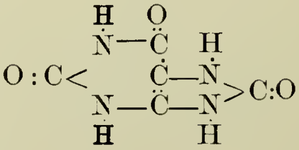
(*a*) *Urea* or *carbamide,*  $O{:}C\begin{smallmatrix}-NH_2\\-NH_2\end{smallmatrix}$, is the most important of the nitrogenous compounds. The average amount is about 33 grammes per day, though with a meat diet it may be twice as great. No portion of the urea is formed in the kidney. That organ is the excretory organ alone. As already stated above, under metabolism, nearly all of the urea is *formed in the liver;* and, for the most part, probably from ammonium carbonate by double dehydration. The source of the ammonium carbonate from the products of katabolism has been discussed above. (See metabolism.)

(β) *Kreatinin* or Glycolyl methyl guanidin or



As has been stated above the kreatinin of the urine probably comes from the kreatin ingested with lean meat. This ingested kreatin is dehydrated in the liver and excreted directly by the kidneys. The fate of the kreatin which is found in the muscles is still a matter of conjecture. The fact that when food is free from kreatin the urine is free from kreatinin would seem to indicate that the sole source of kreatinin is the kreatin of the food. On the other hand the excretion of kreatinin during starvation seems to decrease the force of the preceding observation. The fact that kreatin is present to the extent of 0.3 per cent. in muscle tissue does not necessarily indicate that it is one of the usual mid-products. It may accumulate to the extent indicated above and remain a fairly constant constituent, little being normally added to the supply and little taken away. If it is being constantly formed it is probably completely katabolized to H_2O, CO_2, and NH_3, and the end katabolites built up to the urea level again; or it may be subjected to such a series of changes as that outlined on page 375.

(γ) *Uric acid:* Uric acid is the principal constituent of avian excrement. In the mammalian urine it is an important and constant constituent, though the quantity is small compared with that of urea. The fact that when uric acid is given to a mammal, mixed with food, it is hydrated and oxidized to urea and CO_2 (Emil Fischer, *Ber. d. deutcher Chem. Gaz.*, Bd. 17, 1884) makes it probable that uric acid may be one of the antecedents of urea. That such is the case has not been demonstrated, however. Medicus's formula for uric acid is as follows:



Note that the addition of $2H_2O + 3O$ would reduce this molecule to 2 urea + $3CO_2$. Normal urine contains no free uric acid, but contains several combinations of uric acid with bases: Ammonium urate, sodium urate, potassium urate, calcium urate, lithium urate, etc. Their composition is shown by simply displacing one or more of the hydrogen atoms with the metal. The displaceable hydrogen atoms are indicated by heavier type in the formula. Little is known of the relation which these combinations sustain to the metabolism.

Carnin or Di-methyl uric acid has been found in traces in urine; the two CH_3 radicals displace the two hydrogen atoms indicated above.

Considerable difficulty has been experienced by those who have worked in this field in determining the relations of the metals to the uric acid. To facilitate the explanation of this subject as now understood, we may represent the uric acid formula thus: H_2U; H_2 being the two displaceable hydrogen atoms and U representing the remainder of the uric acid formula: M_2U would represent a *neutral* urate (*e. g.*, Na_2U neutral sodium urate); MHU would represent an acid urate or a *biurate;* $H_2U \cdot MHU$ would represent a hyper-acid salt or *quadriurate.* Neutral urates are decomposed by H_2CO_3 or by carbonates. They cannot then exist in the blood or in the urine. The acid urates (MHU) are very stable salts; they are less soluble than the neutral salts, but much more soluble than uric acid.

Though urine when excreted contains no free uric acid, this appears usually after as a crystalline deposit after the urine has stood, which represents a part of the uric acid freed from the metals. It has been supposed that it was set free by the acid phosphates present in the urine:

$$MHU + MH_2PO_4 = H_2U + M_2HPO_4.$$

Sir William Roberts (quoted by Hopkins, in Schaefer's Textbook, Vol. I., p. 589) believes that the above reaction does not represent completely the situation; "*that uric acid is excreted as a quadriurate; that, being in aqueous solution, the quadriurates are in a state of unstable equilibrium and tend at once to decompose according to the equation:*"

$$\text{(I)} \qquad MHU \cdot H_2U = MHU + H_2U.$$

Thus liberating the uric acid which is precipitated. After this preliminary decomposition the following reaction takes place, in which two molecules of biurate are combined to form one of quadriurate:

$$\text{(II)} \qquad 2MHU + MH_2PO_4 = MHU \cdot H_2U + M_2HPO_4$$

This quadriurate may now be decomposed (I) and the resulting biurate combined (II), and so on until all of the urates are decomposed and the uric acid liberated.

Hopkins calls attention to the fact that it is not demonstrated that equation (I) occurs first. The uric acid may be excreted as a biurate and formed by acid phosphate into quadriurate as shown in equation (II). The two equations could alternate just the same according to this proposition and the uric acid be eventually all liberated.

The amount of uric acid is only about ½ gramme daily on a usual mixed diet. The ratio of uric acid to urea is thus about 1:60. Some have emphasized this ratio as having considerable physiological significance, being a *physiological constant.* A glance at the table giving the composition of urine shows that diet alone may disturb this ratio—with a meat diet the ratio is 1:48—while with a bread diet it is 1:82.

As shown by Camerer (*Zeitsch. f. Biol.*, München, 1896) *the amount of uric acid excreted is a measure of the nucleoproteids ingested.*

The absolute amount of uric acid excreted is "increased by excessive exercise and diminished by rest." (Hopkins.)

Even on the same diet and with the same habits some individuals will excrete a much larger amount of uric acid than others. This individual element must be taken into consideration in clinical cases.

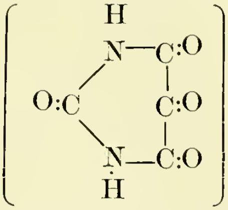
(*δ*) *Hippuric acid* or benzamido-acetic acid, or benzoylglycin:

$$C_6H_5-CO \cdot NH-CH_2-COOH.$$

Under metabolism it was stated that in the system hippuric acid is formed by a synthesis of benzoic acid with glycocoll or amido-acetic acid. We may go a step further and say that when any of the benzole derivatives which contain only one side chain is ingested it is usually oxidized to benzoic acid and this in turn synthesized with glycocoll to form hippuric acid. Such benzole derivatives are toluene, $C_6H_5-CH_3$; cinnamic acid, $C_6H_5-CH \cdot OH-COOH$; phenyl-propionic acid, $C_6H_5-CH_2-CH_2-COOH$. Aromatic bodies of this class are present in epidermal tissues of fruits and vegetables. If one eats apple skins he will increase the excretion of hippuric acid. Hippuric acid then has a double origin: (I) Aromatic bodies in the ingesta; (II) proteid katabolism. The fact that hippuric acid does not entirely disappear from the urine during starvation indicates that the aromatic bodies may result from katabolism of proteids.

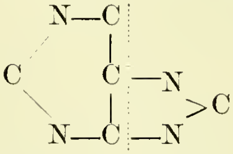
Hippuric acid may combine with metals to form hippurates, in which form it appears in the urine.

(*ε*) *The Xanthin Bodies.*—These bodies, together with uric acid, belong to a group of compounds known as *alloxuric bodies.* They represent the combination of two radicals, *alloxan*

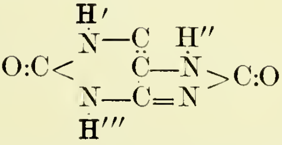


and urea.

Lee gives these bodies the following skeletal structure:



(I) *Xanthin* has the following formula:



The hydrogen atoms printed in heavy type are displaceable atoms.

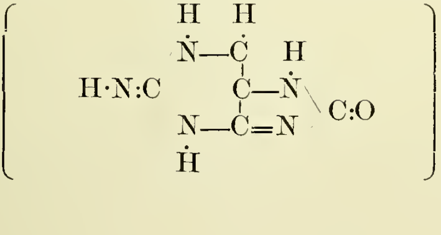
Xanthin arises from the decomposition of nuclein and is found in all tissues and liquids of the body.

(II) *Heteroxanthin* or *Monomethyl Xanthin* ($C_6H_6N_4O_2$) is found in small amounts in the urine. The methyl radical displaces hydrogen atom number one (H′).

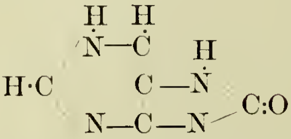
(III) *Paraxanthin, Dimethyl-xanthin* or *Theobromin* is the alkaloid of cocoa. The methyl radicals occupy the positions H′ and H″. This theobromin loses one methyl radical and is excreted as monomethyl xanthin.

(IV) *Trimethyl-Xanthin,* or *Caffein,* or *Thein* is the alkaloid of coffee and tea. The methyl radicals occupy the positions H′, H″ and H‴ and the body is demethylated to mono-methyl-xanthin for excretion. This is the body which imparts to coffee and tea their stimulating effects.

(V) *Guanin,* or *Imido-xanthin* formed by substituting NH for one of the O atoms. This is one of the katabolites of nuclein.



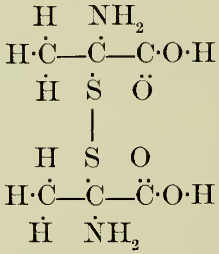
(VI) *Hypoxanthin* or *Sarcin* is next to xanthin the most important xanthin body of the urine. It has one less O than xanthin, hence its name:



(VII) *Adenin* or *Imido-sarcin* is formed by substituting NH for the O. It sustains to the metabolism a relation similar to the other bodies of the group.

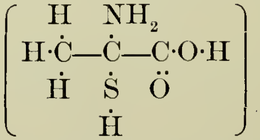
The xanthin bodies arise from the katabolism of nucleo-proteids. When nucleo-proteids are freely ingested uric acid and the xanthins are freely egested. As the metabolic tissues contain nucleo-proteids there is naturally a moderate excretion of the bodies at all times. Normally excreted to the amount of 0.1 per cent. of the total nitrogen (*i. e.*, xanthin nitrogen = 0.1 per cent. total N). The free ingestion of green vegetables raises the nitrogen of the xanthin to 0.6 per cent. of the total nitrogen. In certain forms of leukæmia their amount is greatly increased.

(ζ) *Amido Acids* when ingested are usually katabolized and appear as urea in the urine. But in acute yellow atrophy of the liver and in phosphorus poisoning these bodies pass into the urine unchanged. *Leucin* and *Tyrosin* are the chief amido-acids so excreted. *Cystin*, or *Dithio-diamido-ethidene-lactic-acid* =



$$\begin{array}{rcccccl} & \text{H} & & \text{NH}_2 & & \\ \text{H}\cdot & \dot{\text{C}} & - & \dot{\text{C}} & - & \text{C}\cdot\text{O}\cdot\text{H} \\ & \dot{\text{H}} & & \dot{\text{S}} & & \ddot{\text{O}} \\ & & & | & & \\ & \text{H} & & \text{S} & & \text{O} \\ \text{H}\cdot & \dot{\text{C}} & - & \dot{\text{C}} & - & \ddot{\text{C}}\cdot\text{O}\cdot\text{H} \\ & \dot{\text{H}} & & \dot{\text{N}}\text{H}_2 & & \end{array}$$

This is on its face a double molecule. It is an oxidation synthesis of two cystein molecules: Cystein or Amido-thiopropionic acid



$$\left(\begin{array}{rcccccl} & \text{H} & & \text{NH}_2 & & \\ \text{H}\cdot & \dot{\text{C}} & - & \dot{\text{C}} & - & \text{C}\cdot\text{O}\cdot\text{H} \\ & \dot{\text{H}} & & \dot{\text{S}} & & \ddot{\text{O}} \\ & & & \dot{\text{H}} & & \end{array}\right)$$

is a katabolite of proteid, probably the sulphur-containing katabolite, but it is normally decomposed to simpler products. If not so decomposed it may enter into the following reaction: 2 Cystein $+ O =$ Cystein $+ H_2O$. Cystein is quite insoluble in water and appears in urinary sediment in hexagonal-plate-crystals or it may form calculi. Certain families present the peculiarity of excreting considerable quantities of cystein (0.5 to 1.0 gramme daily).

(*b*) AROMATIC AND NITROGENOUS-AROMATIC COMPOUNDS.—This class of urinary constituents is derived almost wholly from absorbed aromatic bodies. Some of these may exist as such in vegetable tissues, some of them are liberated from or split off from proteid during the digestive and decomposition processes which go on in the alimentary canal. Some of these serve an important office in furnishing a vehicle for the removal of the sulphuric acid; the bodies so formed are called *Conjugated Sulphates*.

There are three subdivisions of this class, viz: (I) Hydroxyl aromatic bodies, (II) Carboxy acids, (III) Conjugated Sulphates.

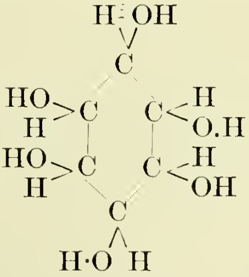
(*α*) *Hydroxyl Aromatic Bodies.*

(I) *Phenol,* oxybenzole, phenyl-hydroxide, carbolic acid: $C_6H_5{\cdot}OH$. (For structural formula see Digestion-Introduction.)

(II) *Kresol,* para-kresol, $C_6H_4 <^{CH_3}_{OH}$. This body is much more abundant than Phenol.

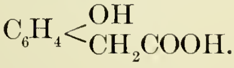
(III) *Pyrocatechin* or ortho-dihydroxybenzole ($C_6H_4 = (OH)_2$), and its isomere *Hydrochinin* or para-dihydroxybenzole $C_6H_4 = (OH)_2$ are both found in human urine; the first only in small quantities; the second only rarely and in traces.

(IV) *Inosit* or hexahydroxybenzole, $C_6H_{12}O_6$. The quantitative formula of this body is very misleading. One would take it for dextrose or at least a carbohydrate. It was so considered until recently. After excessive imbibition of water this body, which seems to be normally present in all the metabolic tissues, will appear in the urine. Its structural formula is as follows:



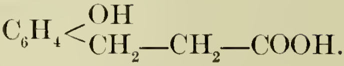
(*β*) *Carboxy acids.*

(I) Para-hydroxyphenyl-acetic acid,



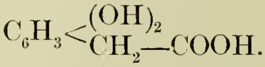
$$C_6H_4 <^{OH}_{CH_2COOH}.$$

(II) Para-hydroxyphenyl-propionic acid,



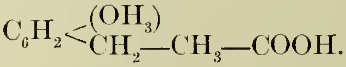
$$C_6H_4<\begin{matrix}OH\\CH_2—CH_2—COOH.\end{matrix}$$

(III) Di-hydroxyphenyl-acetic acid,



$$C_6H_3<\begin{matrix}(OH)_2\\CH_2—COOH.\end{matrix}$$

(IV) Tri-hydroxyphenyl-propionic acid,



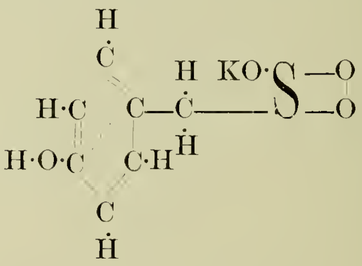
$$C_6H_2<\begin{matrix}(OH_3)\\CH_2—CH_3—COOH.\end{matrix}$$

(γ) *The Conjugated Sulphates.* Incident to the fermentative processes which go on in the alimentary tract phenol, kresol, indol and skatol are formed. These bodies are in part absorbed and pass into the circulation; their accumulation in the blood would be very deleterious to the system. In the liver they meet the acid sulphate of potassium or sodium, or sulphuric acid and enter into a series of harmless combinations which are in due time excreted by the kidneys.

(I) *Phenol sulphate of Potassium* has been discussed above. Phenol may also be conjugated with H_2SO_4 or with $NaHSO_4$.

(II) *Para-kresol-sulphate of Potassium.*

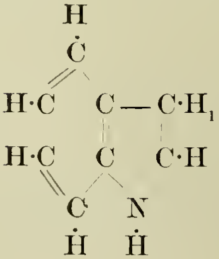
Recall that para-kresol = para-methylphenol and the composition of this body will be at once understood :

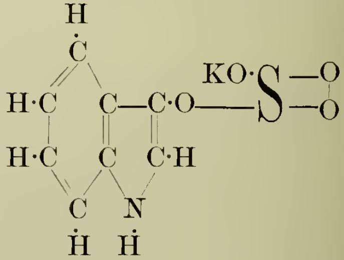


Para-kresol may also be conjugated with H_2SO_4 or with $NaHSO_4$.

(III) *Indoxyl-sulphate of Potassium* or INDICAN.

Indol is one of the katabolites of intestinal fermentation:—

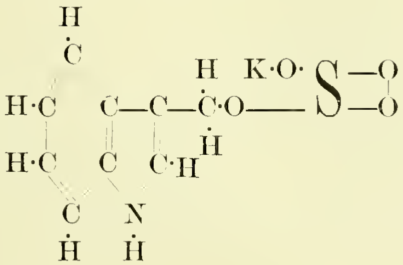




If H_1 be displaced by —OH indoxyl results. The conjugation of $KHSO_4$ with indoxyl results in the formation of indican with the release of H_2O. Indoxyl may also conjugate with H_2SO_4 or $NaHSO_4$.

(IV) *Skatoxyl Sulphate of Potassium.*

Skatol = Methyl-Indol, the H_1 of indol giving place to CH_3. One of the hydrogen atoms of the methyl may be displaced with KSO_4—to form the body in question.



c. The Carbohydrates of the Urine.

(α) *Dextrose.*—The urine of the average individual, living an ordinary life, upon an ordinary diet, generally contains sugar,—dextrose (Hopkins). This normal sugar is *small in amount.* Excessive ingestion of sugar is likely to be followed by a much increased excretion of sugar—*alimentary glycosuria.* In certain diseased conditions—especially in diabetes mellitus—the excretion of dextrose is excessive sometimes exceeding 500 grammes a day,—*pathological glycosuria.*

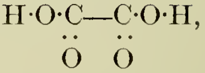
(β) *Lactose* is a normal constituent of the urine of women during lactation. It may be found in minute quantities, and during a portion only of the lactation period. When lactation is suddenly checked the excretion of lactose may be considerable.

(γ) *Pentoses* (*e. g.*, xylose, arabinose) $C_5H_{10}O_5$ appear in the urine after the ingestion of cherries, plums, etc., where pentoses exist as "fruit-gums."

(δ) *Isomaltose* is said to be present in normal urine (Baisch, *Zeitsch. f. Physiol. Chem.*, Bd. XX., S. 249, quoted by Hopkins).

(ε) *Glycuronic Acid*, COOH—$(CHOH)_4$—CHO is derived from glucose by oxidation of the primary alcohol group CH_2OH to the carboxyl group COOH. It is excreted only in traces in the urine, but is generally conjugated with some of the aromatic bodies to form: 1st, Phenol-glycuronic acid; 2d, Indoxyl-glycuronic acid; or, 3d, Skatoxyl-glycuronic acid.

d. Other Organic Compounds.

(*α*) *Oxalic Acids* ($(COOH_2)$), or  $\mathrm{H{\cdot}O{\cdot}\underset{\overset{\cdot\cdot}{O}}{C}{-}\underset{\overset{\cdot\cdot}{O}}{C}{\cdot}O{\cdot}H}$, is a normal constituent of urine. It is supposed to come from ingested vegetable oxalates, though it does not wholly disappear from the urine during flesh diet or during starvation (Marfori—quoted by Hopkins, Schaefer's Text-book, Vol. I., p. 614). It readily forms *calcium oxalate*, which is found in crystalline form in urinary deposits.

(*β*) *The Fatty Acid Series.*—Traces of such volatile fatty acids as acetic, formic, propionic, and butyric acids. They are supposed to be the result of bacterial decomposition in the large intestine. These acids once absorbed are less readily oxidized in the system than the higher members of the same series.

(*γ*) *Urinary Pigments.*—As stated above under (4) *color* the normal color (light yellow) varies in a general way with the relative amount of water present, getting darker with increasing specific gravity. If the color of the urine were due to the presence of one pigment only, it would be possible to contrive a scale of colorimetric tests which might be of considerable clinical value. But there are at least four pigments present and the color of each is different, so that the change of the color of the urine depends upon the relative amounts of these four pigments and is a qualitative change as well as a quantitative one. Thus far attempts at a colorimetric determination have proved of no value. The four urinary pigments now known are: (I) *Urochrome,* (II) *Urobilin,* (III) *Urœrythrin,* (IV) *Hœmatoporphyrin.*

(I) *Urochrome.* This pigment of the urine may be separated by extraction with alcohol, urine which has already been saturated with ammonium sulphate. After the urochrome is removed the urine is almost colorless. The pigment is easily soluble in water. Aqueous solutions of pure pigment have the typical urine color. It seems certain that urochrome is the pigment which more than any other gives the usual color to the urine.

(II) *Urobilin,* as its name implies, is closely related to the bile pigments. It is unquestionably identical with stercobilin, a pigment of the fæces also derived from the bile. It is found in the bile which has undergone partial decomposition without access of air. It seems to be identical with hydrobilirubin, though this has not been demonstrated. Hydrobilirubin is derived from bilirubin by hydration and reduction.

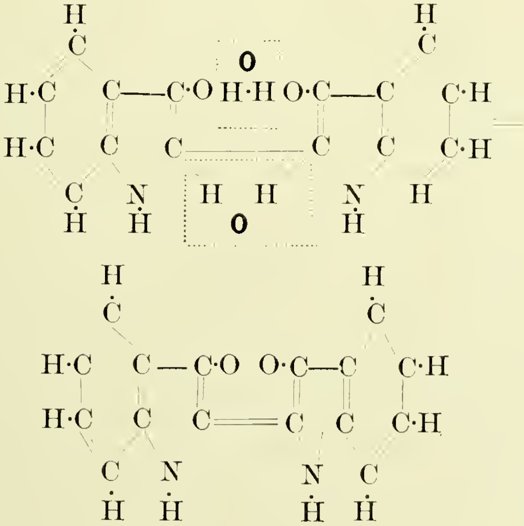
$$C_{32}H_{36}N_4O_6 + H_2O + H_2 = C_{32}H_{40}N_4O_7$$

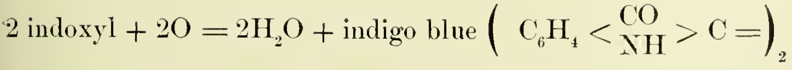
$$\text{Bilirubin} + H_2O + H_2 = \text{Hydrobilirubin or } \textit{Urobilin.}$$

(III) *Uroerythrin* is the pigment which colors urinary deposits pink. It exists in normal urine in traces only. Neither physiological nor pathological importance has been ascribed to this pigment.

(IV) *Hæmatoporphyrin* ($C_{32}H_{32}N_4O_5$) is present only in traces in normal urine, but may become an important constituent in certain pathological urines.

(V) *Chromogens* are present in the urine and the use of reagents for general analytical purposes may cause the appearance of some pigment which may be confusing if not understood. *Indoxyl* is a chromogen which easily oxidizes to indigo blue or its isomere indigo red. The following equation represents the reaction[1]:





$$2 \text{ indoxyl} + 2O = 2H_2O + \text{indigo blue} \left(C_6H_4 < {CO \atop NH} > C = \right)_2$$

Oxidizing agents added to the urine may give rise to either or both of these pigments (indigo blue, indigo red). But the addition of nitric acid readily decolorizes these pigments by further oxidation.

Pathological urines may contain normal pigments in abnormal quantities or such abnormal urinary pigments as: *Hæmoglobin, methæmoglobin, bilirubin, biliverdin, carboluria,* etc.

2. **Inorganic Constituents of the Urine.**—(*a*) ACIDS.—(*a*) *Sulphuric acid and its compounds* are excreted to the extent of 2 to 2.5 grammes per diem on a mixed diet and as low as $1\frac{1}{4}$ grammes on a bread diet. (See table of urinary constituents.) The sul-

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[1] The added oxygen atoms are represented in heavier type.

phur is ingested as a constituent of the proteids. The excreted sulphur is in part ($\frac{1}{5}$) combined in such forms as cystin, possibly also sulpho-cyanides, and bilary taurin (pathologically), but most of it ($\frac{4}{5}$) is in the form of sulphates. Of these the conjugated sulphates, discussed above under aromatic compounds, comprise 10 per cent., while the inorganic sulphates comprise 90 per cent. The inorganic sulphates are Na_2SO_4, $NaHSO_4$, K_2SO_4, and $KHSO_4$.

(β) *Phosphoric acid and its compounds* are excreted to the extent of about 3 grammes daily on an average diet. This quantity is somewhat increased by a meat diet and reduced to about half as much on a bread diet. There are phosphates present in abundance in vegetable foods, but they are mostly in insoluble forms (unabsorbed) forms. There are phosphates of Ca and Mg; but most of the phosphoric acid is combined with Na and K.

To the acid sodium phosphate (NaH_2PO_4) the urine owes its acid reaction. Calcium phosphate may form a characteristic portion of the deposit from feebly acid urine; while the triple phosphates of magnesium and ammonium frequently separate out in crystals which take the forms of "feathery-stars" or "coffin-lids." Phosphates are decreased in nephritis and are increased in certain neuroses.

(γ) *Hydrochloric acid* is chiefly combined with sodium. In this form the major portion of chlorine is absorbed and excreted; the integrity of the sodium chloride molecule being usually unimpaired during the metabolic processes. The amount of NaCl in the circulating fluid remains fairly constant. An increased ingestion of this salt is followed by an increased excretion of it. NaCl seems to be retained in the system during febrile conditions and to be excreted more freely after the condition becomes normal.

(δ) *Other acids* (I) *Carbonic acid* is present in acid urine and carbonates in alkaline urine; (II) *Nitric acid* combined as nitrates which are not products of metabolism but are ingested with the food.

(*b*) *Bases.*

(α) *Sodium* in common salt is used so freely by many as a condiment that its excretion may vary within wide limits; 5 grammes per diem is the amount given by Hopkins as average. Parkes in the above table gives more than twice that much. This difference is undoubtedly due to individual differences in the use of salt with the food. This metal is excreted mostly as a chloride, but also as a sulphate and a phosphate.

(β) *Potassium* varies very much with the diet, being much more abundant with a meat diet than with a vegetable diet.

(γ) *Calcium* and (δ) *Magnesium* are both present in considerable quantities in the food, but as they are in insoluble forms (phosphates) a small amount only is absorbed. These salts are important in bone-making and tooth-development, and are therefore found in abundance in both milk and eggs. Hoppe-Seyler (*Zeitsch. f. physiol. Chem.*, 1891, Bd. XV., S. 161, Quoted by Hopkins) found that the excretion of calcium salts is much more abundant during rest than during exercise.

2. THE PROCESS OF URINARY EXCRETION.

a. Glomerular Excretion.

1. **Experiment.**—It has been discovered that the newt has, in common with several other amphibia, a double renal circulation. The glomeruli are supplied by the renal venæ portæ, branches from the femoral vein.

Experiment (I). Inject sugar (or any crystalline and easily diffusible substance) into the blood. It will reappear in the urine. Tie the renal arteries, the sugar will cease to be excreted. *Conclusion:* Sugar is thrown out of the blood by the glomeruli.

Experiment (II). Inject urea into the blood. It will be excreted. Tie the renal arteries. The urea will continue to appear in abnormal amounts.

Experiment (III).—Inject a mixture of sugar and urea. Both will be excreted. Tie the renal artery: Sugar will cease to be excreted, but the urea will continue to appear in abnormal amounts; thus the results of experiments (I) and (II) are confirmed.

This series of experiments was first performed by *Nussbaum*. From these experiments and many others we may accept it as conclusively demonstrated that *the glomeruli excrete the water and easily diffusible salts.*

2. **Factors Influencing Glomerular Excretion.**—(*a*) It Varies with Blood-pressure.—But blood-pressure varies as the heart-force—terminal resistance remaining the same—or, as terminal resistance, the heart-force remaining the same.

(*b*) *It varies with the fullness of the vascular system.* (I) increased after copious drinking of water; (II) decreased after copious perspiration. Now this increase or decrease of water occurs without any essential change in blood-pressure; therefore the glomeruli must have an independent action other than filtration.

(*c*) *Diuretics* act by modifying some one of these factors: (I) Digitalis, by increasing heart-force. (II) The nitrites, by causing local dilatation of vasæ efferentia, and, therefore, increased local pressure. (III) Caffein and many other drugs, however, stimulate the glandular activity of the epithelium of the convoluted tubules, and, therefore, increase the urea, uric acid, etc., of the urine without appreciably varying the volume. Lauder Brunton, of Oxford, urges the great importance of distinguishing two classes of diuretics: 1st, Those which stimulate glomerular excretion of water and salts, and, 2d, Those which stimulate glandular excretion of the poisonous urea, etc.

(*d*) But, as convenient as it is to believe that the process of glomerular excretion is one of simple *filtration, i. e.*, varies exactly as the pressure, we are forced by numerous observations and experiments to believe that some other factor or factors are at work in the process. Any condition which increases the pressure, but at the same time decreases the velocity, will decrease the rate of excretion of water. A partial occlusion of the renal vein has the effect of increasing pressure and decreasing velocity. A complete occlusion of that vein stops water excretion and injures the organ so that a removal of the occluding ligature is followed by a copious excretion of albuminous urine. It is supposed that the high pressure in the glomerulus mechanically stops filtration by pressing the glomerular epithelium against the walls of the Bowman's capsule; further, that this pressure and tension on the glomerular epithelium injures it so that it is no longer able to perform a selective activity, and lets serum albumin filter through. On the whole, it is concluded (Hermann's *Handbuch der Physiologie*, B. V., S. 338) that it is rather *increase* in *velocity* than simple increase in pressure, which is the *essential factor*.

b. Glandular Excretion or Excretion by the Epithelium of the Convoluted Tubule.

Experiments of Nussbaum produce practically conclusive evidence that the epithelium of the convoluted tubule is the seat of the excretion of urea and allied bodies. Von Wittich observed that in birds, whose urine contains little water, urates may be detected microchemically in the epithelium of the tubules, but not in Bowman's capsule. If the kidneys be extirpated the urea and allied bodies accumulate in the blood; therefore, these bodies are not formed by the glandular cells of the convoluted tubules; these cells only "separate them out of the blood" and excrete them. We cannot properly speak of the secretion of urine by the kidneys, but rather the excretion.

The influence of the nervous system upon the activity of the kidney in excretion seems to be not perfectly made out. All of the facts can be explained by assuming that the fibers of the renal plexus (see Introduction to Excretion) are vaso-motor and not secretory. The kidney is influenced on the one hand by local blood-pressure and on the other by the constituents of the blood. In the case of the active cells of the kidney as in the case of the intestinal cell we must ascribe a selective function. Dextrose and urea circulate side by side. The cells of the kidney let urea pass. They do not normally let any appreciable amount of dextrose pass.

c. The Egestion of Urine—Micturition.

The urine passes from the pelvis of the kidney through the ureters to the bladder, where it is retained until that viscus is sufficiently full to stimulate its sensory nerves and so appeal to the consciousness of the individual. The act of micturition consists in voiding the urine in response to this "appeal of nature." The act is partly voluntary and partly involuntary. The initiatory act is voluntary and consists in relaxation of the sphincter whose tonic contraction retains the urine between the egestive acts. Once the sphincter is relaxed the contraction of the involuntary muscular coats of the bladder is sufficient to empty the viscus, though this force may be supplemented by contraction of the abdominal walls. The final act is the voluntary contraction of the *accelerator urinæ* muscle.

The innervation of the bladder is from two sources: (I) From the lower dorsal and upper lumbar via the mesenteric ganglion and the hypogastric nerves. Stimulation of these causes contraction of the circular fibers of the bladder and the sphincter. (II) From the second and third sacral via the nervi erigentes. Stimulation of these causes relaxation of the sphincter and contraction of the detursor urinæ.

B. PULMONARY EXCRETION.

Of the products of excretion practically all of the CO_2, about one-sixth of the water and minute quantities of certain organic materials are excreted by the lungs, and leave the body in expiration. For the details of this subject see RESPIRATION.

C. CUTANEOUS EXCRETION.

Excretion is only an incidental function of the skin and is secondary to *protection,* to *general sensation* and to *thermolysis.* That this is true is evident from the fact that the sebaceous glands secrete fatty products whose function is to keep the skin pliable and non-absorbent, while the other glands—the sweat-glands—produce a fluid which is almost wholly water and whose primary function is the regulation of heat by facilitating heat radiation (thermolysis). The reciprocal relation between the amount of water which leaves the body by the kidneys and that which leaves the body by the sweat glands is an evidence that the skin must not be ignored as an organ of excretion.

1. THE SWEAT.

a. General Characters.

1. **Quantity.**—The amount of sweat formed in a day varies between very wide limits; the minimum being about 500 grammes and the maximum being about 2000 grammes for 24 hours, though it may reach a rate of 4000 grammes per diem for an hour or more in an experiment. To collect the excretion for experimental purposes the subject's arm or leg may be enclosed in a rubber bag; or the subject may be placed naked in a ventilated chamber, as in the experiments of Voit and Pettenkoffer. In such an experiment Schierbeck (*Archiv f. Physiol.*, Leipzig, 1893, S. 116; Quoted by Reid in Schaefer's Text-book, Vol. I., p. 671) found with progressively increasing temperature a progressively increasing excretion of water and of CO_2.

Excretion of H_2O and CO_2 by Skin at Various Temperatures of Surrounding Air.

Temperature of Chamber.	H_2O Excretion. (Grammes per hour)	H_2O Excretion. (Grammes per 24 hours.)	CO_2 Excretion. (Grammes per hour.)	CO_2 Excretion. (Grammes per 24 hours.)
29.8°C.	22.2	532.8	0.37	8.9
30.4° "	27.8	667.2	0.40	9.6
31.5° "	71.9	1725.6	0.37	8.9
32.8° "	73.4	1761.6	0.35	8.4
33.8° "	82.6	1982.4	0.87	20.9
35.4° "	106.8	2563.2	1.04	25.0
38.4° "	158.8	3811.2	1.23	29.5

2. **The Specific Gravity** of human sweat is from 1003 to 1006; the greater the quantity the lower the specific gravity.

3. **The Reaction** of sweat is acid, though when the excretion is copious it may become neutral or even alkaline in reaction. The acidity is due to $NaHPO_4$. On standing the reaction changes from acid to alkaline due in part to the change of urea to ammonium carbonate.

b. Chemical Composition of Sweat.[1]

Sweat	100.00
Water	98.88
Solids	1.12
(1) Organic	0.66
(*a*) Fats and Fatty acids	0.41
(*b*) Epithelium	0.17
(*c*) Urea and other Nitrogenous compounds	0.08
(2) Inorganic	0.46
(*a*) Sodium Chloride	0.28
(*b*) Other Salts	0.18

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[1] From Charles' Physiol. Chemistry, p. 349; Quoted by Halliburton: Text-book of Chem. Physiology, p. 820.

1. **The Organic Constituents of Sweat.**—These are in excess of the inorganic, but not so much in excess as in the case with urine.

(*a*) THE FATS AND FATTY ACIDS are largely derived from the secretion of the sebaceous glands, but when the sweat is collected from the palm of the hand it still contains a small amount of fats and volatile fatty acids. The reaction of the sweat is in part due to the presence of fatty acids. The volatile fatty acids present are : formic, acetic, propionic, butyric, caproic.

(*b*) THE EPITHELIUM is carried away mechanically. The epithelial scales are composed chiefly of *keratin*, of which sulphur is an important constituent. This is one of the ways in which the sulphur leaves the body.

(*c*) UREA AND OTHER NITROGENOUS COMPOUNDS have been demonstrated by Argutinsky (*Archiv f. d. ges. Physiol.*, 1890, Bd. XVI., quoted by Reid, S. 594) to be present in the sweat ; in one case finding 0.363 grammes of urea in 226 c. c. sweat collected in half an hour. According to Reid the nitrogen excreted by the skin may equal 4.7 per cent. of that by the urine. This amount is greatly increased in uremic conditions. Uric acid, kreatinin, etc., have also been found.

2. **The Inorganic Constituents of Sweat.**—These are made up chiefly of *sodium chloride*. *Among other salts* are : potassium chloride, acid sodium phosphate, sodium and potassium sulphates, calcium and magnesium phosphates. The salts are thus qualitatively equivalent to those of the urine.

2. THE PROCESS OF CUTANEOUS EXCRETION—PERSPIRATION.

1. **The Influence of the Nervous System upon Cutaneous Excretion.**—The sweat-glands are provided with (*a*) *secretory*, and (*b*) *vaso-motor* nerves ; the latter are represented by both *constrictor* and *dilator* fibers. The secretory fibers radiate from a center (or probably several centers), in the central nervous system—cord and medulla. The centers are stimulated directly ; (I) by a highly venous condition of the blood ; (II) by a high temperature of the blood ; (III) from the cerebrum ; (IV) by poisons : pilocarpin, strychnia, nicotine, etc. The centers are stimulated reflexly by subjecting the skin to a high temperature.

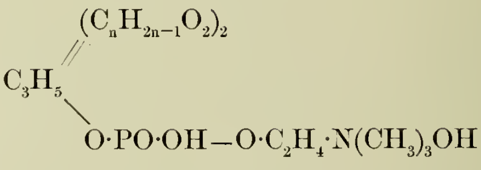
2. **Factors which cause a Variation in the Quantity of Perspiration.**—The total perspiration—500 grammes to 2 kilogrammes daily—either evaporates as it is formed—*insensible perspiration*, or it collects upon the surface of the skin—*sensible perspiration.*

The total amount of perspiration varies (I) with the temperature of the air, (II) with the proportion of water in the blood, (III) with blood-pressure, (IV) with the velocity of the blood-flow, arising usually from muscular activity, (V) with the activity of kidneys and bowels, (VI) with the state of the emotions, (VII) with general systemic conditions—certain diseases are accompanied by profuse diaphoresis, (VIII) individual peculiarity, (IX) drugs (pilocarpin). In variables (I) to (V) an increase of the variable causes an increase of the perspiration. In (VI) anything which causes the skin to flush is likely to be accompanied by perspiration, though there is a "cold sweat" also which may accompany fear.

The amount of *sensible perspiration* will depend primarily upon all of the factors which cause a variation in the total amount of perspiration, and secondarily upon the condition of the atmosphere, being increased by higher temperature and decreased by increasing the capacity of air for moisture.

D. INTESTINAL EXCRETION.

Of the various fluids and solids poured into the alimentary canal by the surrounding or tributary glandular epithelium, by far the greater part is to be considered to be typically *secretion,* for it is introduced into the lumen of the canal to serve a particular purpose; after serving that purpose it may be reabsorbed or passed out with the egesta. There are, however, certain substances which must be recognized as excretions: (α) *The Bile Pigments:* (I) Bilirubin; (II) Biliverdin; (III) Hydrobilirubin (Stercobilin); (β) *The Fat-like Constitutents of the Bile:* (I) Cholesterin ($C_{26}H_{43}OH$), (II) Lecithin,



$$C_3H_5\begin{cases}(C_nH_{2n-1}O_2)_2 \\ O\cdot PO\cdot OH - O\cdot C_2H_4\cdot N(CH_3)_3OH\end{cases}$$

Lecithin and cholesterin are constituents of nerve tissue. They must be looked upon as nerve katabolites and the liver the organ for the excretion of those katabolites which are peculiar to nerve tissue. (γ) *Salts.* Certain salts, calcium salts especially, of the bile and of other intestinal liquids must be looked upon as on the way out of the system.

DIVISION *B.*

THE PHYSIOLOGY OF THE EXTERNAL RELATIONS: THE MOTO-SENSORY ACTIVITIES.

Chapter IX. THE DERMAL SYSTEM: PROTECTION.
Chapter X. SENSATION.
Chapter XI. PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM.
Chapter XII. PHYSIOLOGY OF THE MUSCULAR SYSTEM.

CHAPTER IX.

THE SKIN: THE DERMAL SYSTEM.

INTRODUCTION.

1. SUMMARY OF THE MORPHOLOGICAL FEATURES OF THE DERMAL SYSTEM. THE HISTOGENESIS AND HISTOLOGY OF THE SYSTEM.
2. THE GLANDS OF THE DERMAL SYSTEM.

THE PHYSIOLOGY OF THE DERMAL SYSTEM.

1. PROTECTION.
2. THERMOLYSIS.
3. EXCRETION.
4. RESPIRATION.

THE SKIN: THE DERMAL SYSTEM.

INTRODUCTION.

The skin may be looked upon as an organ. Those structures indissolubly associated with the skin both histogenetically and functionally may, with the skin proper, be called the *Dermal System.*

This system of organs represents histogenetically epiblast proper and dermal mesenchyme; the former giving origin to those tissues and organs which are distinctively dermal, and the latter furnishing the substratum upon which these distinctive structures are built or supported. Functionally the dermal system is *par excellence*, the system of *external relations*, which fact has a definite relation to the histogenesis, the epiblast coming from the ectoderm of the gastrula.

1. SUMMARY OF THE MORPHOLOGICAL FEATURES OF THE DERMAL SYSTEM.

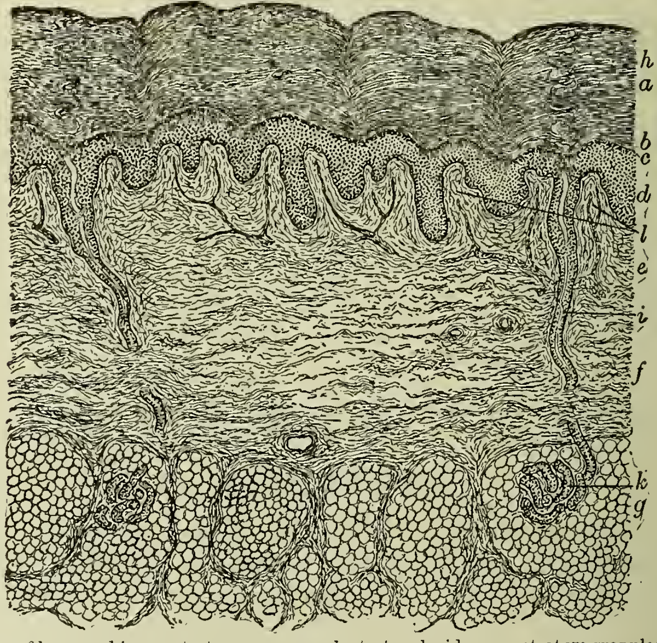
From a physiological standpoint the following points regarding the structure of the skin and its associated organs are of importance:

The dermal system of organs involves, without exception, (*a*) mesenchymal tissues as foundation, and (*b*) an epiblastic surface as superstructure.

a. The Dermis or Corium.

The Mesenchyme may be represented by the close-felted corium with its blood vessels and lymph vessels; by the dentine of a tooth, or by the dense transparent substance of the cornea. (See Fig. 204, *e*, *f*.)

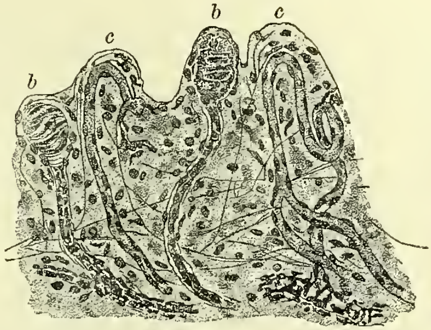
Fig. 204.



Section of human skin: *a*, stratum corneum; *b*, stratum lucidum; *c*, stratum granulosum; *d*, stratum Malpighii; *e*, *f*, papillary and reticular layers of corium; *g*, stratum of adipose tissue; *h*, *i*, spiral and straight portions of duct of sweat-gland; *k*, coiled portion of sweat-gland; *l*, vascular loops occupying papillæ of corium. (Piersol.)

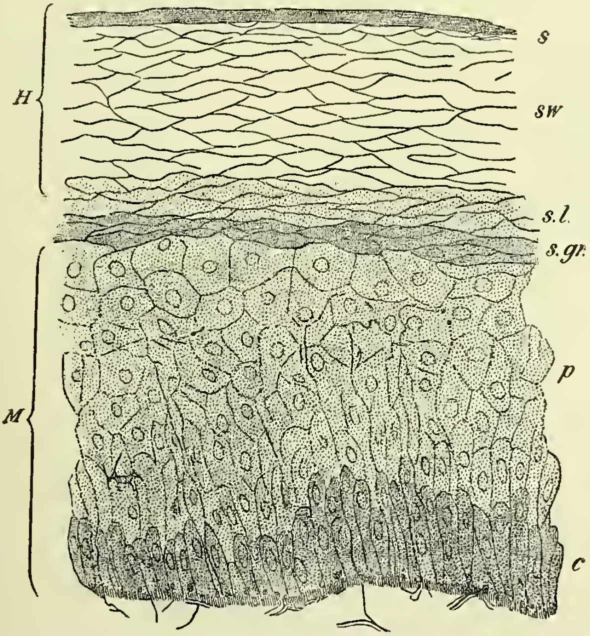
The mesenchymic dermis, or true skin is everywhere beset with minute papillæ (Figs. 204, 205). The papillæ are very vascular (Fig. 208) and through more or less specialized nerve-endings they are especially sensitive (Fig. 205). These papillæ are variously modified in structure in different parts of the dermal system; they form the basis of a hair follicle (Fig. 209), they form the basis of the nails (Fig. 207), and of teeth. Within them are located the special tactile corpuscles. In a further modification they form the lingual papillæ (*q. v.*). The marked vascularity of the papillæ facilitates the support of the tissues which are associated with them in the formation of hair, nails, teeth, etc. The nerve supply insures the extreme sensitiveness of the dermal tissues enumerated: teeth, hair, nails; but it is the root or matrix which is sensitive, not the hair, nail, or tooth itself.

FIG. 205.



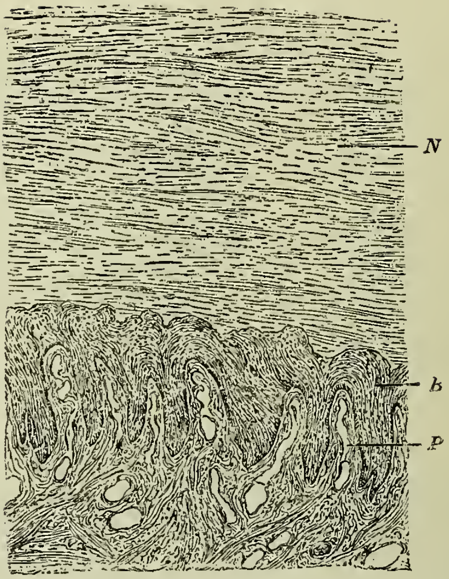
a, nerve fiber; *b*, tactile papillæ, containing a Meissner tactile corpuscle; *c*, vascular papillæ. (After BENDA.)

FIG. 206.



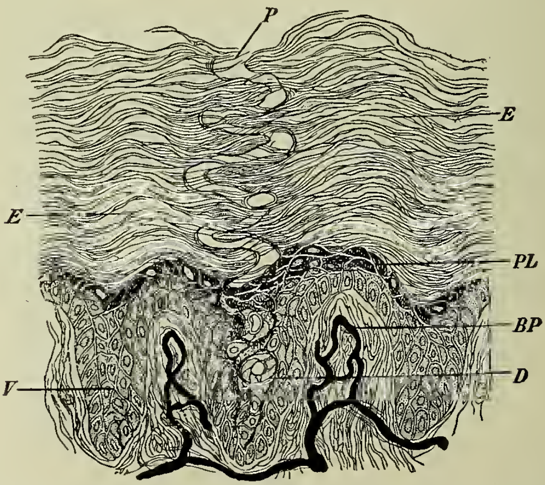
Section of epidermis. *H*, horny layer, consisting of *s*, superficial horny scales; *sw*, swollen-out horny cells; *s.l.* stratum lucidum; *M*, rete mucosum or Malpighian layer, consisting of *p*, prickle-cells, several rows deep; *c*, elongated cells forming a single stratum near the corium; and *s.gr.*, stratum granulosum of Langerhans, just below the stratum lucidum; *n*, part of a plexus of nerve-fibers in the superficial layer of the cutis vera. From this plexus fine varicose nerve-fibrils may be traced passing up between the epithelium-cells of the Malpighian layer. (SCHAEFER after RANVIER.)

FIG. 207.



Section across the nail and nail-bed. (100 diameters.) *P*, ridges with blood vessels; *B*, rete mucosum; *N*, nail. (SCHAEFER after HEITZMANN.)

FIG. 208.



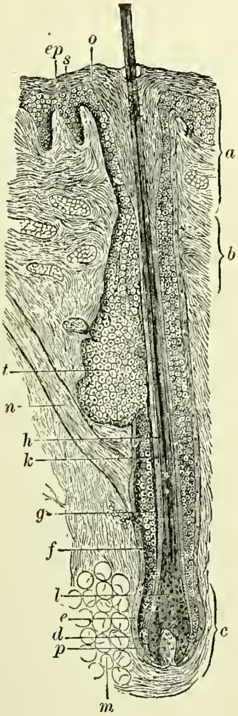
Duct of a sweat-gland passing through the epidermis. (Magnified 200 diameters.) *BP*, papillæ with blood vessels injected; *V*, rete mucosum between the papillæ; *E*, stratum corneum; *PL* stratum granulosum; *D*, sweat-duct, opening on the surface at *p*. (SCHAEFER after HEITZMANN.)

b. The Epidermis.

[The epiblast may be represented by the cuticle of the skin, by the imbricated scales which compose a hair, by the active cells of the cutaneous glands, by the enamel of the teeth, or by the delicate cuticle which covers the cornea or the tympanic membrane. (See Fig. 204, *a*, *b*, *c*, *d*.)

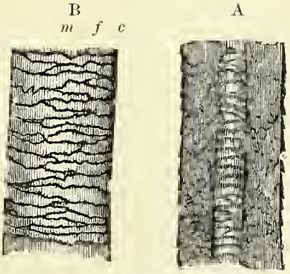
The epiblast presents a series of layers whose cells are generated by karyokinesis at the surface of the corium from the columnar or cuboidal cells of the stratum malpighii (Fig. 206). The constant formation of new cells at this level pushes out the older cells which through loss of water and through other physical and metabolic changes die, and become insensible, horny scales. The particular form and aggregation of these horny

FIG. 209.



Hair-follicle in longitudinal section. *a*, mouth of follicle; *b*, neck; *c*, bulb; *d*, *e*, dermic coat; *f*, outer root-sheath; *g*, inner root-sheath; *h*, hair; *k*, its medulla; *l*, hair-knob; *m*, adipose tissue; *n*, hair muscle; *o*, papilla of skin; *p*, papilla of hair; *s*, rete mucosum, continuous with outer root-sheath; *ep*, horny layer; *t*, sebaceous gland. (SCHAEFER after BISSIADESKI.)

FIG. 210.



Piece of human hair. (Magnified.) A, seen from the surface; B, in optical section. *c*, cuticle; *f*, fibrous substance; *m*, medulla, the air having been expelled by Canada balsam. (SCHAEFER.)

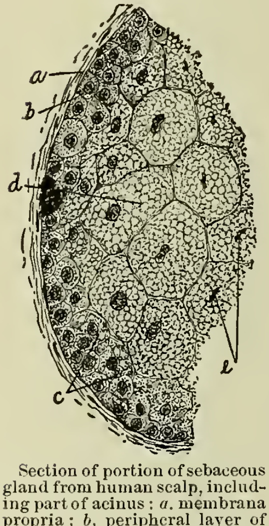
scales differ much in different locations. On the general cutaneous surface they are simple dry scales which are constantly shed; on the hair (Figs. 209 and 210), teeth, or nails (Fig. 207), there is an accumulation which takes a distinctive form and which serves as an organ of protection, defence or offense, and is only periodically shed or is worn off to keep pace with growth (or conversely). In the case of man the hair and nails are usually artificially cared for, the occupation of man not usually wearing the growth away fast enough.

2. THE GLANDS OF THE DERMAL SYSTEM.

a. Protective Glands.

α. **The Sebaceous Glands** are present over the whole surface of the body except the soles of the feet, the palms of the hands, the dorsal surface of the third phalanges (see Fig. 211). The ducts of the glands open at the roots of the hairs on all hairy surfaces, but on the lips, the prepuce and the corona of the glans penis the ducts open free upon the surface. The secretion of the sebaceous glands is called sebum.

Fig. 211.



Section of portion of sebaceous gland from human scalp, including part of acinus: *a*. membrana propria; *b*, peripheral layer of cuboidal cells; *c*, elements in which fatty metamorphosis is beginning; *d*, cells filled with fatty particles and exhibiting marked intra-cellular networks; *e*, nuclei of cells. (Piersol.)

Specialized forms of the sebaceous glands are: (i) *Preputial glands*, whose secretion—the *smegma preputii*—differs from sebum in containing substances which give it a characteristic odor. Musk is from the preputial gland of the musk deer. (ii) *Anal glands*, which are only slightly modified in the human subject may be strongly modified in other mammalia. In the otter, hyena, and civet the anal glands secrete a modified sebum which serves for sexual attraction. In the skunk the secretion serves for defense. (iii) The *meibomian glands* are slightly modified sebaceous-glands which open upon the edge of the eyelid; the oily surface thus produced prevents the overflow of tears. (iv) *The Uropygial Glands* of many birds is a specialized sebaceous gland. The oil which it secretes is spread upon the feathers by the bird and serves to protect the feather-coat against absorption of water. (v) *The Lachrymal Gland* whose secretion keeps the delicate mucous membrane of the conjunctiva moist and freed from dust, belongs to the dermal system, and to the protective glands of that system, though morphologically they are more closely related to the salivary glands.

b. Secretory Glands.

The mammary glands, unquestionably dermal glands, may have been derived phylogenetically from sweat glands. The secretion formed and the method of its formation makes the laetiferous glands clearly analogous (if not homologous) to the sebaceous glands. (See *Lactation* under *Reproduction.*) Pigeons possess lactiferous glands which are clearly sebaceous glands and are tributary to the crop. This "pigeon milk" contains fat, a proteid clotting with rennet, globulin, salts, and water.

c. Excretory Glands.

The sweat glands (Fig. 211). See Cutaneous Excretion.

THE PHYSIOLOGY OF THE DERMAL SYSTEM.

1. PROTECTION.

The skin, being the organ of external relations, must necessarily stand between the general organism and its environment.

a. The Nerves of the Skin.

The skin is provided with sensory nerve-ends; this lends to protection in putting the animal on guard against various dangers. Some of these sensory areas are highly specialized, *e. g.*, the cornea and lens, admitting light to the retina; the taste buds,—facilitating the access of solutions to the gustatory nerves; the moist nasal epiblast facilitating the influence of odors upon the olfactory nerves.

b. Dermal Protective Structures.

The skin is provided with various structures for special protection against mechanical injury, *e. g.*, the nails protect the finger-tips and toe-tips; hair protects the organism against mechanical injury,—witness its cultivation for that purpose by football players,—it serves a more important office, however, in protection again cold. In this connection may be mentioned the further protection of the eye by the lids whose periodical winking during working hours and continued closing during sleeping hours serve to protect the eye against dust and drying. The eyelashes protect the eye against bits of solid matter that might otherwise strike the eye. The brows shed off the perspiration. All of these protective structures are dermal. The teeth are, however, more distinctly prehensile and offensive than defensive; though the dermal teeth of sharks are defensive and protective and the oral teeth are the homologues of the dermal teeth. (See Digestion,—introduction, comparative.)

c. The Sebaceous Glands.

The skin is provided with oil glands or sebaceous glands whose function is to secrete oil for the hair and cuticle, keeping both soft and pliable and especially non-absorbent. As indicated in the introduction the oil glands may take various specialized forms as for offense, defense, or sexual attraction. The chemical composition of the sebum is not very well known, because the normal cutaneous secretion is not formed in sufficient quantity for analysis. The cheesy contents of a distended sebaceous cyst consist of water 31.7 per cent., epithelium and nucleo-albumin (casein) 61.7 per cent., fat 4.2 per cent., fatty acids 1.2 per cent., salts 1.2 per cent. In the typical secretion the proportion of fat and fatty acids is probably much greater and that of epithelium and nucleo-albumin[1] much smaller. The *fat* consists of a mixture of *glycerine fats*, with whose composition the reader is familiar, and of *cholesterin fats*. Cholesterin is a monatomic alcohol having the formula $C_{27}H_{45}OH$. Cholesterin fat of palmitic acid is $CH_3—(CH_2)_{14}—COO{\cdot}C_{27}H_{45}$. The *fatty acids* consist, according to Schmidt, of butyric, valeric, and caproic acids. It is to the fatty acids that secretion owes its distinctive odor. Free *cholesterin* and isocholesterin are present.

Two especially interesting facts regarding the sebum are: First; *the cholesterin fats resist putrefaction, i. e., they resist the use of the skin as a culture field for bacteria.* Second, the homology of the mammary glands with the sebaceous glands receives an extra element of probability in the fact that the *nucleo-albumin of the sebum is casein.*

2. THERMOLYSIS.

The common cutaneous surface, with its vascular cutis vera and its sweat glands, forms the *organ* of *Thermolysis.* Just how the skin governs the rate of heat elimination is discussed in full under Animal Heat.

3. EXCRETION.

Third in importance among the functions of the skin is excretion. Here is an instance where an excretion performs an important office incident to its final exit from the body. Every gramme of water which evaporates on the surface of the skin eliminates 582 calories of heat, or takes that much away from the body.

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[1] The identity of the nucleo-albumin with casein is questioned by Weymouth Reid, but is not questioned by Halliburton and others.

It is evident that *Excretion* and *Thermolysis* are intimately associated. The greater the occasion for free evaporation of water incident to thermolysis, the greater the excretion of water by the skin. But if there is a given amount of water to be eliminated from the system, it is evident that the other water-eliminating organs must give off correspondingly less water. Such is the case; after profuse perspiration the urine is less voluminous and more highly colored. Conversely, a marked decrease of perspiration will be occasion for a marked increase of the volume of urine, which will be more watery. Not only is there a *reciprocity,* there is also a vicarious relation between skin and kidneys. When one is disabled the other performs as much as possible of the function of the disabled organ.

4 RESPIRATION.

In many of the lower animals, particularly in amphibia, the skin is an important organ of respiration. The moisture of its surface facilitates the exchange of gases by diffusion in these animals.

In the higher vertebrates respiration is an unimportant function of the skin.

CHAPTER X.

SENSATION. INTRODUCTION.

A. GENERAL SENSATION.

1. SUBJECTIVE.

2. SUBJECTIVE-OBJECTIVE.
   COMMON SENSATION.
      (*a*) *Hunger.*
      (*b*) *Thirst.*
      (*c*) *Suffocation.*
      (*d*) *Fatigue.*
      (*e*) *Pain.*
      (*f*) *Shivering.*
      (*g*) *Tickling.*
      (*h*) *Sexual Sensation.*

3. OBJECTIVE.
   I. THE TACTILE OR PRESSURE SENSE.
   II. THE POSTURE SENSE.
      (*a*) *Sense of Equilibrium.*
      (*b*) *Muscular Sense.*
   III. THE TEMPERATURE SENSE.

B. SPECIAL SENSATION (OBJECTIVE): THE SPECIAL SENSES.
   IV. SMELL.
   V. TASTE.
   VI. HEARING.
   VII. SIGHT.

SENSATION.

INTRODUCTION.

EVERY animal organism is provided with organs which make the cerebral sensory centers cognizant of certain conditions and changes of the environment. In other words, certain conditions of the environment act as stimuli to more or less specialized peripheral organs. The effect of a stimulus is transmitted along an afferent nerve to the brain, where it so affects the cerebral centers as to cause a consciousness of the stimulus,—*a sensation.* Through intercentral action between the sensory centers and the higher cerebral centers the animal sums up the sensations received from an object making a complete conscious *perception.* An interpretation of perceptions producing not only a mental picture of an object and its properties, but giving the animal an idea of the relation of the object under consideration to other objects, is called a *conception.*

Note that a conscious sensation involves *attention*; that perception involves *memory*; and that conception involves *reason*. The clearness of the sensation, perception and conception is proportional to the attention, memory and reasoning involved in them. Sensation furnishes pabulum for all higher forms of mental activity.

The ectoderm is the embryonic layer which gives rise to the peripheral organs of sensation as well as to the sensorium. The specialized epithelium of the sense-organs is from the epiblastic division of the ectoderm, while the sensorium is from the neuroblastic division of that layer.

It will be profitable at this point to express in tabulated form the relations between the specific stimuli of the environment, the more or less specialized peripheral sense-organs which receive the stimuli and the special sensations aroused in the sensorium. (Table: See next page.)

Note that there is a departure from the time-honored classification of the senses as: "Five: Feeling, taste, smell, hearing and seeing." The first one of these has, under careful investigation, been resolved into several distinct senses, one classification of which is given in the table.

Sensory nerve-endings may be classified, on the basis of structure, into specialized and non-specialized. The specialized nerve-endings, those enumerated in the table, below the dash,—are those which seem to be especially adapted structurally for response to particular stimuli. For example, the structure of the retina, exceedingly complex and highly specialized, seems to be especially adapted to receive the light, while the organ of Corti, just as complex, seems to be especially adapted to receive sound. Moreover, the retina is sensitive to light only of all the stimuli of the environment, or if there is a response to any other kind of energy it always affects the sensorium as light. In the same way sound alone of all the stimuli of the environment affects the organ of Corti. Another structural distinction is found in the fact that the specialized nerve-endings are all located in particular organs also especially adapted to receive the special stimulus; for example, the refractive media of the eye focus the light upon the retina, and the muscles of the eye direct the organ toward the source of light. The non-specialized nerve-endings are more or less widely distributed over the surface of the skin and mucous membranes. They are not located in specialized organs and are not evidently adapted to receive special stimuli. It may be that the "tactile cells and corpuscles" are the end-organs of *touch and muscular sense*, and it may be that the filamentous endings or the end-bulbs are the end-organs of the temperature sense; but these distinctions, if they exist, remain yet to be demonstrated.

Showing Relations Between Stimuli, Sensory Nerve-Endings and Sensations.

	General Stimuli.	Special Stimuli.	Sensory Nerve-Endings.		Sensation.
Conditions of the Environment.	Mechanical.	Pressure. Tension.	Filamentous Endings.		*A.* General Sensation. Common Sensation. *a.* Hunger. *b.* Thirst. *c.* Suffocation. *d.* Fatigue. *e.* Pain. *f.* Shivering. *g.* Tickling. *h.* Sexual Sensation. Objective Sensation. I. Tactile or Pressure Sense. II. Posture Sense. *a.* Muscular Sense. *b.* Sense of Equilibrium. III. Temperature Sense.
			Tactile Cells.	Simple Compound or Corpuscle of Grandry.	
			Tactile Corpuscles.	Spherical End-bulbs Genital Corpuscles. Meissner's "	
	Thermal:	Heat.	End-Bulbs.	Cylindrical End-Bulbs. Paccinian Corpuscles	
	Chemical.	In Gaseous Medium.	Olfactory Nerve Endings.		*B.* The Special Senses. IV. Smell.
		In Liquid Medium.	Gustatory Nerve Endings.		V. Taste.
	Vibration of Ponderable Matter.	Sound:	Auditory Nerve Endings: Organ of Corti.		VI. Hearing.
	Vibration of Imponderable Matter.	Light:	Optic Nerve Endings: Retina.		VII. Vision.

Sensations may be classified into three categories on the basis of the source of the stimulus:

1. Sensations which are the immediate result of the reaction of the organism to the conditions of the environment: Pressure sense, posture sense, temperature sense, smell, taste, hearing, vision. Because these sensations are caused by objects wholly outside of the organism they are called *Objective Sensations.*

2. Sensations in which the immediate source of the stimulus is within the organisms, though the ultimate source is in the environment. An example of this class of sensations is *hunger.* Something within the organism produces a conscious call for nourishment. This may be so urgent as to occasion considerable discomfort, merging into actual pain if not satisfied. The ultimate cause of hunger is in the environment, but the stimulus cannot be classified with the general or special stimuli enumerated in the accompanying table. *Thirst* and *weariness* also belong clearly to this class of sensations. *Pain* and *sexual sensation* may belong to this class or to the preceding. In these two sensations the stimulus may be mechanical and may be traced more or less immediately to the environment. This class of sensations may, for want of a more concise term, be called *Objective-Subjective sensations.*

3. Sensations which accompany dreams, hypnosis, hysteria, and various states of the central nervous system and which merge from the perfectly normal into the pathological. These sensations are just as real to the subject as are the objective sensations, but an observer traces no connection to an external stimulus. This class of sensations are called *Subjective Sensations.* They partake of the nature of a memory of previous sensations, but they are more than that. A subjective sensation is an actual *re-experiencing of a former sensation.*

THE PHYSIOLOGY OF SENSATION.

A. GENERAL SENSATIONS.

The term general sensations is used to include a class of sensations excluded by the well-defined *special senses, i. e.,* the general senses are those with no specialized peripheral organs.

1. SUBJECTIVE GENERAL SENSATIONS.

This class of sensations has been sufficiently discussed above.

2. OBJECTIVE-SUBJECTIVE SENSATIONS.

For the definition of this class see the Introduction.

a. Hunger. *b.* Thirst. *c.* Suffocation.

These three sensations are Nature's admonitions to supply the organism with solid, liquid or gaseous nourishment. The greater the urgency for satisfaction of the need the greater the discomfort when it is not satisfied. The animal organism can live only a short time without oxygen. When the supply of oxygen is cut off the sensation of suffocation begins within a few seconds and increases rapidly in intensity, passing very soon into a paroxysm of the most agonizing pain ending in convulsions and death if the need is not supplied.

Next to oxygen in urgency is the need for water. If there is little perspiration the thirst may be mild for 24 hours. As soon as the sensation of thirst becomes thoroughly fixed upon the consciousness of the animal nothing can dislodge it. The discomfort becomes more and more intense until death supervenes.

The animal organism can do without food for many weeks if all activity can cease. Bears hibernate for several months. Indians accustom themselves to 48- and 72-hour fasts in order to be able to endure without much discomfort the exigencies of war and the chase. To those who are accustomed to three regular meals each day the missing of one meal is likely to cause considerable discomfort, but the feeling is one of emptiness rather than of real hunger. If one fill the stomach with water the discomfort soon disappears and real hunger begins to appear in a variable time afterwards. Hunger and thirst are in the healthy individual infallible signs of the needs of the organism. These senses may, however, become perverted, or, at least, the actual sensation may be misinterpreted. For example, a child with an overfilled stomach may call for more—having misinterpreted the vague feeling of discomfort in the gastric region for hunger.

d. Fatigue. *e.* Pain.

These two sensations apprise the organism of over-stimulation. Moderate over-stimulation is followed by a feeling of fatigue. Nature is requesting a rest. Excessive over-stimulation leads to a feeling of actual pain. Nature is *demanding* a rest. The most usual occurrence of weariness is after muscular or nervous activity; the most usual occurrence of pain is after stimulation of some of the peripheral end-organs by some of the external stimuli: pressure, tension, heat, cold, chemical energy, sound or light. But pain may be purely subjective sensation, having no apparent connection with objects outside of the organism but arising from certain conditions in the central nervous system. Some painful sensations may be accurately localized, while others are localized in a most general way only. The more acute the tactile sense of a part, the more accurate the localization of pain in the part. Pain is the most general of all sensations. Some contend that there is a special set of nerves to convey the sensation of pain together with certain other sensations. But the fact that every sensation of which the brain may be conscious and every activity of which the organism is capable may be accompanied by pain, and the fact that abnormal conditions of the system may be accompanied by pain makes it highly improbable that any particular set of nerves is to be looked upon as *pain nerves*. Pain is distinctly a common sensation.

f. **Shivering.** *g.* **Tickling.** *h.* **Sexual Sensation.**

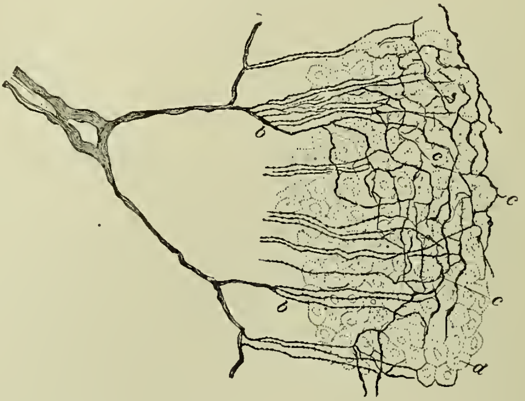
These sensations have certain features in common. They all begin in definite objective sensations and partake of the nature of *after-sensation*. If the cold points of a considerable area are stimulated so that the superficial tissues become chilled the shivering sensation is induced. Once started it is likely to continue some time after the local reaction has occurred. Moreover the sensation frequently occurs when there is no objective cause; *i. e.*, it may have its origin in the central nervous system. Tickling sensation is usually caused by a light stimulation of the tactile nerve-endings, but in many individuals the sensation may be aroused by "make-believe" movements on the part of another, or even an active imagination may induce the sensation. Tickling may have its origin in the central nervous system. Sexual sensation may be stimulated peripherally by mechanical stimuli or centrally. In fact, the most effective stimulus is the central one. If the stimulation be carried to the point of the final, culminative sensation (orgasm) this is to be looked upon as the *indirect after-sensation* and not the *direct objective sensation*, and it is the indirect after-sensation which belongs to the category of the heading.

3. OBJECTIVE GENERAL SENSATION.

Preliminary to a discussion of the general sensations of the periphery one may profitably review the structure of the sensory nerve endings. These endings may be classified as non-specialized and specialized. The *non-specialized* are called *filamentous* and are distributed to the skin, cornea and mucous membranes (see Fig. 212). *The specialized sensory nerve endings* represent three genera: tactile cells, tactile corpuscles, and end-bulbs. Figures 213 and 214 represent *simple and compound tactile cells*. The simple tactile cells differ from the filamentous endings in having a discoidal termination associated with a slightly modified epithelial cell. The compound tactile cell lies within the epidermis of the mammalian or avian skin. Note the discs and the two or three cells enclosed in a sheath.

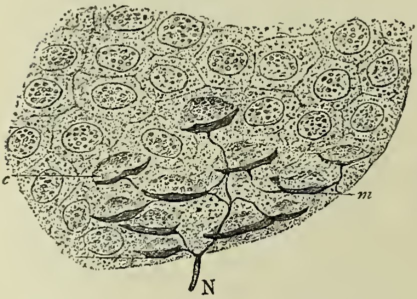
The *tactile corpuscles* are located in the corium of skin and mucous membrane. The *spherical end-bulbs,* shown in Fig. 215 are found in the conjunctiva and other mucous membranes of man. *The genital corpuscles* (Fig. 216) are found upon the glans penis, the glans clitoris and other associated surfaces in mammals in general. The *tactile corpuscles* of Meissner are located as shown in Fig. 217, in papillæ of the corium upon the palms of the hands, the soles of the feet and upon the volar surfaces of fingers and toes in man. The complex internal structure of these bodies is

Fig. 212.



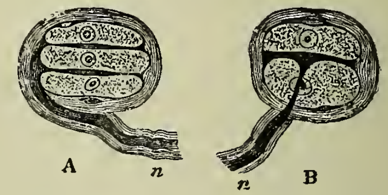
Intra-epithelial nerve-termination in the anterior epithelium of the cornea, as seen in an oblique section. *a*, an axis cylinder; *b*, sub-epithelial nerve-fibrillæ; *c*, intra-epithelial network; *d*, epithelial cells. (Klein.)

Fig. 213.



Special nerve-endings within the epidermis; gold preparation: N, nerve-fiber entering the epithelium and dividing into the fibrils which are connected with the tactile disks (*m*); upon these latter rest the tactile cells, *c*. (Piersol after Ranvier.)

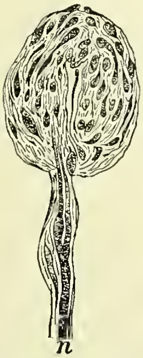
Fig. 214.



Compound tactile cells from the duck's tongue. (Izquierdo.) A, composed of three cells, with two interposed disks, into which the axis-cylinder of the nerve, *n*, is observed to pass; in B there is but one tactile disk inclosed between two tactile cells. (Schaefer.)

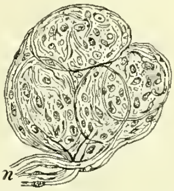
shown in Fig. 218. There can be little doubt that these specialized sensory nerve endings are the organs of touch, if it is admissible to call them organs. Of the several species of end-bulbs only one will be given,—*The Pacinian body* (Fig. 219). These structures are widely distributed in mammals. They occur in sub-cutaneous tissue along the nerves supplying the skin, especially

Fig. 215.



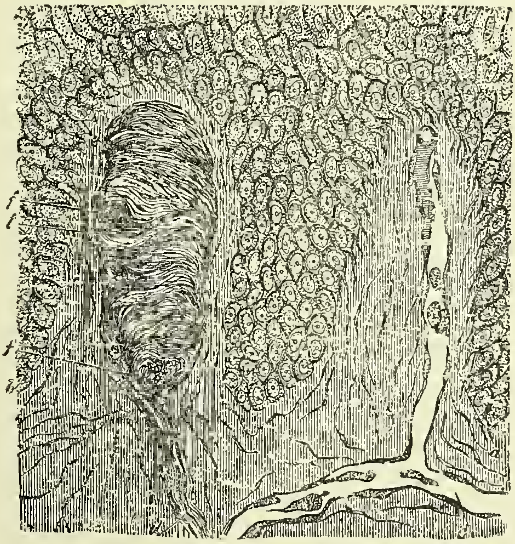
Simple spherical end-bulb from the human conjunctival mucous membrane: *n*, the medullated nerve-fiber which disappears within the capsule. (After Krause.)

Fig. 216.



Genital corpuscle from the human clitoris; this ending represents a group of partly fused simple spherical end-bulbs: *n*, nerve-fibers entering the capsule. (Schaefer after Krause.)

Fig. 217.

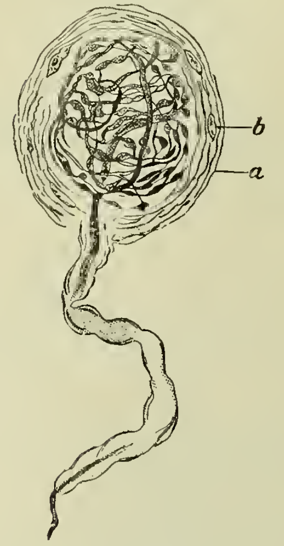


Section of skin showing two papillæ and deeper layers of epidermis. *a*, vascular papilla with capillary loop passing from subjacent vessel, *c*; *b*, nerve-papilla with tactile corpuscle, *t*. The latter exhibits transverse fibrous markings; *d*, nerve passing up to it; *f*, *f*, sections of spirally winding nerve-fibers. (Schaefer after Biesiadecki.)

of the hands and feet, the external genitalia, the joints of the extremities, periosteum of certain bones, the peritoneum.

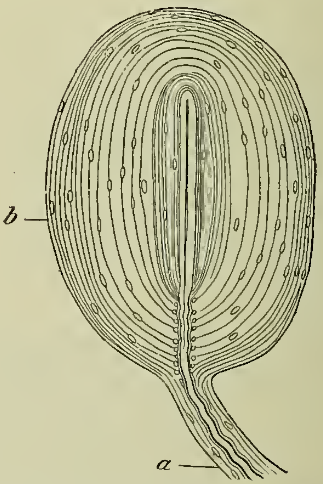
The various structures just described receive at the periphery various sensations. The fact that the tactile corpuscles of Meissner are most numerous in those locations where the tactile sense is most acute justifies the conclusion that these structures represent peripheral receptive tissues for mechanical stimuli; but does not justify the conclusion that none of the other sensory nerve endings respond also to various mechanical stimuli. It is probable that some of the endings described respond to mechanical stimuli and some to thermal. The mechanical stimuli may be further subdivided, some of them in the form of pressure affect the cutaneous and articular surfaces, while others in the form of varying tension affect the tendons and muscles. The varying tension of the tissue may affect the nerve-endings as varying pressures, however. Further, the thermal stimuli are to be subdivided: bodies lower in temperature than the skin stimulate certain nerve endings, while bodies of higher temperature stimulate other nerve endings. Whether these nerve-endings differ from each other structurally

FIG. 218.



Meissner's corpuscle from the human corium. *a*, upper portion, in which the epithelial cells alone are represented. The nuclei of those cells are in the broader peripheral portion of the cytoplasm; *b*, nerve-dendrite coiled about the epithelial cells; *c*, nerve-fiber. (BÖHM and DAVIDOFF.)

FIG. 219.



A Pacinian corpuscle from the mesentery of the cat. *a*, the medullated nerve-fiber; *b*, the concentric capsules. (KLEIN.)

as well as functionally or differ only functionally is unknown. In short the sensations classified in the above table are the result of the stimulation of some one or more of the sensory nerve-endings enumerated in the opposite brace; this is all that can be said with certainty at present.

I. THE TACTILE SENSE: THE SENSE OF TOUCH.

In man this sense is most acute in the finger tips, the lips, and the tongue. In quadrupeds the sense is most acute in the lips, tongue or proboscis. This sense alone brings to one only an idea of the state of the substance—whether it is solid, liquid or gaseous; of the surface of a solid—whether it is smooth or rough, and if the latter the particular character of the roughness; whether it is oily or sticky, or whether it is bounded by curved surfaces or by planes, edges, or angles, or a combination of these features. The character of a liquid may be determined, whether it is light, limpid like water, or heavy like mercury, or whether it is gelatinous, viscous, slimy or oily. The only character of a gas that appeals to the tactile mechanism is the negative one that it affords no resistance to the movements of hands or fingers. The sum of the knowledge which may be derived through touch alone is greater than that which may be derived through any other one sense. Experience derived from both touch and sight will enable one to *infer* from lights and shades and lusters what touch would definitely reveal. One instinctively verifies these inferences by touching the object with the fingers. The tactile sense is used in two different ways: first, to announce to the central nervous system when some resistant object touches the surface of the body; second, to investigate the properties of certain objects of the environment. In the first the organism is passive, in the second it is active. The first is a means of protection, the second a means of adding to one's knowledge. A similar classification of function may be made for all of the objective sensations. In serving the first one of these purposes the tactile mechanism must be able to differentiate stimulation of different portions of the periphery. It is not enough to know that some sharp point is touching the surface of the body, but to avoid injury it is important to know just where the point is. This is accomplished by what is called the *power of localization.* Through this power the central nervous system is conscious, *e. g.*, that in a particular location a sharp point is touching the periphery. This knowledge enables the organism to protect itself from unnecessary injury. The tactile mechanism is also endowed with the *power to estimate pressure.* Those portions of the skin most acute in their tactile sensibility are, at the same time, most acute in their power of localization, but not in their power to estimate pressure. This has led to two methods of testing the tactile sense: one to measure the power to estimate pressure, and the other, the power of localization.

To test the pressure sensibility one places upon a certain cuticular area a series of weights of exactly the same surface of contact and approximately the same temperature. Such experiments have revealed the facts that the parts most sensitive to pressure are the forehead, the temples, the back of the hand and the flexor surface of the forearm. In these localities 2 mgm. can be felt, while the finger tips can not feel a weight of less than 5 to 15 mgm.

Regarding the power to differentiate increments in the weights used as stimuli it may be said that: *the greater the inital stimulus the greater the increment must be in order to be discernible.* This is the basis for Weber's law: "*The amount of stimulus necessary to provoke a perceptible increase of sensation always bears the same ratio to the amount of stimulus already applied*" (cited by Sewall in the American Text-book of Physiology, p. 836). Fechner studied this same problem and reached similar results which he formulated in his "psycho-physical law": "*The intensity of sensation varies with the logarithm of the stimulus.*" That is, if a series of stimuli represent the intensities: 10:100:1000:10000, the sensations would represent the intensities 1:2:3:4. These laws hold in the main for medium stimulation; for very light or very strong stimulation they do not hold, the *sensation being more acute for moderate stimuli.* Another law of Weber (*Hermann's Handbuch der Physiologie*, Bd. III., 2, S. 336) may be thus formulated: *If two equal weights have different areas of contact the one that touches the larger surface feels the heavier.*

The Power of Localization is tested by use of the æsthesiometer which is similar to a pair of dividers or draftsman's compass. In using the instrument the points are lightly touched to the surface of the skin. The greater the acuteness of tactile sense, or the more acute the power of localization the nearer the points may be brought together and yet be felt as two points. Beyond a certain minimum distance the points can no longer be distinguished as two, but feel like one point.

The following table shows results of tests which were made to determine whether all points are equally sensitive and especially whether symmetrically located points on the same individual are equally sensitive.

Showing variations of symmetrically located points on the same individual. From this table one is justified in three inferences:

1. Symmetrically located points in the human body may not possess the same acuteness of tactile perception.

2. There is a very great variation in the acuteness of sensation in different parts of the cutaneous surface of the same individual.

3. The more acute the tactile perception of a part the more likely it is to vary in acuteness from its laterally homologous point.

TABLE I. OF TACTILE SENSIBILITY.

Point of Observation.	Individual A.		Individual B.	
	Right.	Left.	Right.	Left.
Tip of Tongue.	1.2 mm.	1.2 mm.	1.2 mm.	1.2 mm.
Palm of 3d Phalanx.	2.0	2.5	2.00	1.5
" " 2d "	3.75	3.25	3.5	3.5
Tip of Nose.	5.5	5.5	8.0	8.0
Back of 2d Phalanx.	9.0	11.0	9.9	8.0
Back of Hand.	15.0	20.0	17.0	22.0
Forearm.	24.0	24.0	42.0	42.0
Sternum.	32.0	32.0	42.0	42.0
Back.	66.0	66.0	77.0	77.0

Tests upon a number of individuals yielded the results recorded in Table II., showing not only the variations of tactile sensibility in different parts of the same individual, but also the variations of different individuals.

TABLE II.

SHOWING DEGREES OF TACTILE SENSIBILITY OF CUTANEOUS SURFACE OF BODY.

Portion of the Body Tested.	Man. mm.	Boy æt 13. mm.	Woman. mm.	Man. mm.
1. Tip of tongue.	.7	1.	.6	.8
2. Middle of dorsum of tongue.	1.1	1.1	1.	1.6
3. Center of hard palate.	1.6	4.	2.3	1.1
4. Under lip (red surface).	.7	2.1	1.7	2.1
5. Upper lip (" ")	1.3	1.2	1.5	3.
6. Tip of nose.	4.	2.	1.2	2.5
7. Tip of chin.	5.	6.	6.	2.8
8. Cheek over malar bones.	5.	4.	4.	6.5
9. Lobe of ear (ventral surface).	4.5	6.7	8.2	5.6
10. Neck (ventral surface).	3.	4.1	3.1	5.8
11. Neck (dorsal surface).	2.2	3.7	1.8	5.4
12. Neck (lateral surface).	2.2	3.2	2.9	5.4
13. Forehead.	5.1	4.9	4.3	5.2
14. Tips of fingers.	1.	1.1	1.4	1.
15. Palmar surface of second phalanges of fingers.	1.1	2.	3.8	1.6
16. Dorsal " " " " " " (transverse).	5.	3.2	3.6	1.1
17. " " " " " " " (longitudinal).	7.5	3.	6.1	5.
18. Palmar surface of hand.	2.1	3.2	4.2	2.3
19. Thenar hypothenar eminences.	.8	2.1	4.2	2.2
20. Dorsum of hand (longitudinal).	5.6	4.3	6.5	8.6
21. Dorsal surface of forearm.	5.7	4.5	5.3	5.
22. " " " upper-arm.	4.8	4.7	5.3	5.2
23. Dorsum of hand (transverse).	4.7	2.8	4.2	6.
24. Flexor surface forearm.	3.3	3.2	4.5	2.8
25. Flexor surface upper-arm.	5.8	4.7	4.5	1.7
26. Dorsum of foot.	12.	15.	19.	24.
27. Flexor surface of thigh (transverse).	36.	30.	34.	33.
28. Calf of leg.	15.	23.	21.	30.
29. Lateral dorsal region.	38.	35.	37.	40.
30. " sacral "	30.	28.	31.	32.
31. " cervical region.	35.	32.	39.	37.
32. Mid sacral region (over spine).	13.	16.	13.	15.
33. " dorsal " " "	10.	13.	17.	11.
34. " cervical " " "	12.	14.	15.	10.
35. Flexor surface thigh (longitudinal).	64.	57.	61.	69.

Table II. justifies the following conclusions:

1. There is very great variation in the acuteness of perception in different parts of the same individual.
2. There is considerable variation in the acuteness of tactile perception in different individuals.
3. When the points determine a line which is transverse to the axis of a limb they may be distinguished as TWO at a much smaller distance than is the case when the line is parallel to the axis of the limb.
4. The tactile sense is best developed in persons whose senses in general are well developed, for example, Mr. Z, a laboring man was compared with Miss X in twelve points of observation and she uniformly excelled him. But not in tactile sense alone did Miss X excell Mr. Z. Her sense perceptions in general were more acute.
5. The further one goes from the tips of fingers, toes or tongue, the less acute is the tactile perception.
6. The least sensitive parts of the body are those subject to more or less constant pressure, the epidermis is, in such locations, very thick.
7. The tactile sensibility is much more acute on all flexor surfaces than upon the corresponding extensor surfaces. For evidence see Table III.

TABLE III.

Flexor Surfaces.		*Extensor Surfaces.*	
Over Pectoralis Major.	20 mm.	Over Scapula.	32 mm.
Umbilical Region.	18 "	Dorsal Region.	53 "
Neck (ventral).	11 "	Neck (dorsal).	15 "
Arm.	15 "	Arm.	17 "
Forearm.	7 "	Forearm.	11 "
Wrist.	7 "	Wrist.	9 "
Thigh.	45 "	Thigh.	53 "
Leg.	9 "	Leg.	15 "
Average.	16.5		25.6

II. THE POSTURE SENSE.

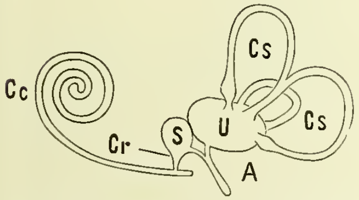
The organism is provided with a mechanism through which it is made continually conscious not only of the general position of the body in space, but of the relative position of different parts of the body. The consciousness of general position in space is called the sense of equilibrium, the consciousness of the position of different parts of the body is inseparable from muscular sensation; and is probably incidental to it. These two sensations together give the organism a clear consciousness of its position or posture; *i. e.*, gives the *Posture Sensation.*

a. The Sense of Equilibrium.

The maintenance of equilibrium is of prime importance both in animal locomotion and in all positions of rest except that of absolute relaxation in a decumbent position. The whole mechanism of equilibrium includes the nicely adjusted muscular action required to hold head and body poised upon the base of support, and it includes the sensation necessary to make the central nervous system cognizant of any disturbance of the poise. This sensory part of the mechanism is the one now under consideration. The principal end-organ of equilibrium seems to be the system of semicircular canals connected with the inner ear. If this were the only end-organ the sense of equilibrium might probably be classed as a special sense. But the complete sensation of equilibrium is a combination of sensations from various sources; it might, in fact, be called, rather, a *perception of equilibrium*, rather than a simple sensation. (See Introduction.) The sensory nerves from the soles of the feet, from the ischial skin when sitting, from the muscles and tendons, from the articular surfaces, and from the eyes all bring sensations which contribute to the general sensation or *perception of equilibrium.* If any part of the mechanism is disabled the equilibrium is in part impaired. The parts intact may by especial activity cover the deficiency in the mechanism, but though the equilibrium may be apparently perfect the sense of equilibrium is not perfect.

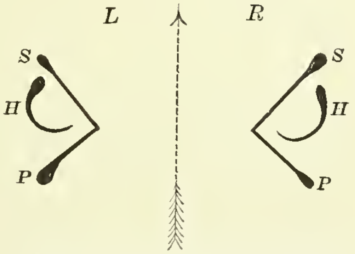
In this place we may discuss those features of the semi-circular canals which especially fit them for end-organs for the perception of the position of the axis of the body in space. Fig. 220 shows the membranous labyrinth with its three canals, two saccate structures and the cochlea. Note: (I) That each canal has an enlargement near one end—the ampulla; (II) That the three canals lie in different planes.

FIG. 220.



Membranous labyrinth. Cs, semi-circular canal; U, utriculus; S, sacculus; A, aqueduct of vestibule; Cr, ductus reuniens; Co, cochlea.

FIG. 221.

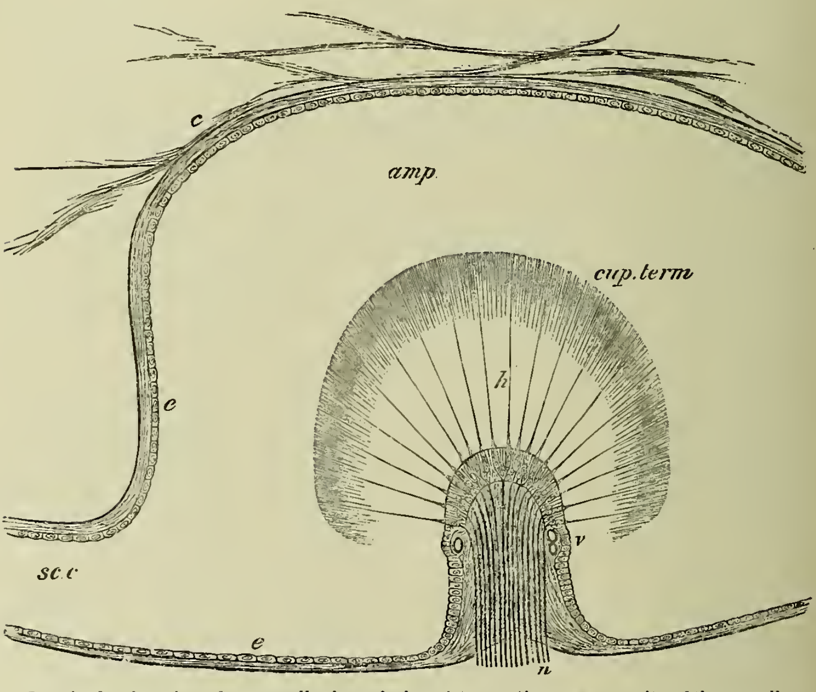


Diagrammatic horizontal section through the head to illustrate the planes occupied by the semi-circular canals. (WALLER.)

Fig. 221 gives Waller's diagram showing certain important space relations of the canals. Note (III) That the superior canal of the right side lies in a plane parallel to that of the posterior canal of the left side, while the left superior plane is parallel to the right posterior plane, and the two horizontal planes are parallel; (IV) That the six planes represent the three dimensions of space; (V) That the ampullæ of any pair of parallel canals are at opposite extremities of the canal,—*e. g.*, the ampulla of the left superior canal is opposite to ampulla of the right posterior canal.

Fig. 222 shows the minute structure of the *crista acustica* of an ampulla. The long, delicate bristles are epiblastic in their origin. Note (VII) that each specialized epithelial cell is intimately connected with a branch of the vestibular nerve (see Fig. 223), and that the bristles are really agglutinated structures, each formed of several fibrillæ (see Fig. 223, *h′*); (VIII) that the saccule and the utricule are each provided with a small specialized surface similar to that of the crista.

FIG. 222.

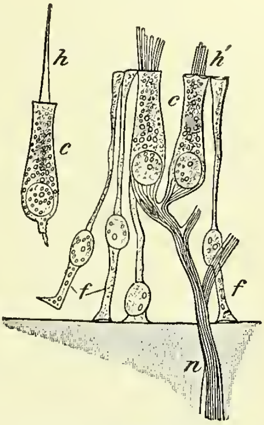


Longitudinal section of an ampulla through the crista acustica. *amp.*, cavity of the ampulla; *sc.c.*, semi-circular canal opening out of it; *c*, connective tissue attached to the wall of the membranous ampulla and traversing the perilymph; *e*, *e*, flattened epithelium of ampulla; *h*, auditory hairs projecting from the columnar cells of the auditory epithelium into the cupula, *cup. term.*; *v*, blood vessels; *n*, nerve-fibers entering the base of the crista and passing into the columnar cells. (SCHAEFER.)

If the head or the whole body be rotated upon its antero-posterior axis in the direction from left to right, the endo-lymph of the right horizontal canal will flow toward the ampulla of the canal where the pressure would increase, while the endolymph of the left horizontal canal will flow away from the ampulla of that canal, tending to decrease the pressure. According to the hypothesis of Crum-Brown, fairly confirmed by experiment this difference of pressure is the efficient stimulus. Other movements of the head, or of the body as a whole, affect other pairs of semicircular canals in a way similar to that indicated above.

Through this mechanism and its center in the cerebellum the individual is made conscious of every position and every change of position of the head in space. If in an animal one of the semicircular canals be opened, the animal has the sensation which accompanies fall of pressure in that canal, and makes efforts to compensate it by "*forced movements*," which really carry the animal's body in the direction opposite to that in which it feels it is turning. Such observations have seemed to confirm the hypothesis of Crum-Brown, which is now generally accepted. Lee (*Jour. of Physiol.*, XVII., p. 192) looks upon the saccule and utricle as the organs of *static equilibrium*, in which, when the animal is at rest, the weight of the otoliths under gravitation stimulates the maculæ acusticæ. The fact that in fishes these structures are highly developed seems to confirm Lee's hypothesis, for in these animals there is no supplementary cutaneous stimulation like the solar or ischeal stimulation in man, and the fish must depend entirely upon these structures for its sense of position.

FIG. 223.



Auditory epithelium from the macula acustica of the saccule of an alligator. (Highly magnified.) *c*, *c*, columnar hair-cells ; *f*, *f*, fiber-cells ; *n*, nerve-fiber, losing its medullary sheath and apparently terminating in the columnar auditory cells: actually, however, the nerve-fibrils arborize around these cells ; *h*, bristle or hair ; *h′*, base of hairs, split up into fibrils. (SCHAEFER after RETZIUS.)

b. The Muscular Sense.

Supplementary to the sense of position in space is the sense of muscular tension. If one stand erect and as still as possible with the heels together he will not be conscious of any essential change of equilibrium yet he will be conscious of a slight variation of the distribution of weight upon the soles of the feet and especially conscious of variations in tension of different sets of muscles and tendons involved in the maintenance of the erect position. If one fix a tracing point to the head and stand under a horizontal tracing surface so adjusted as to record any change of position it will be noticed that the position of the point changes from moment to moment—never returning exactly to the starting point except sometimes by accident. As a general rule the taller the subject the greater the amplitude of his oscillations. A study of these tracings and of the sensations which one experiences while standing erect indicate that such a position is maintained particularly through the muscle sense. One is conscious at one time of a greater tension upon, say, the muscles of one side of the body than upon those of the other, and is conscious at the same time of a slight change of the direction of the body axis. A moment later he is conscious of a greater tension upon the sets of muscles which before were less tense and conversely. The muscles are in a state of mild tonic contraction constantly, but the tension of any one group of muscles varies continually, the action being so coördinated as to maintain the body erect within very narrow limits. One has not the sensation of losing and regaining the balance, but he has the sensation of shifting of pressures upon the soles of the feet, also of changing of tension in muscles and tendons so that one may say that the coarse adjustment of equilibrium is effected through the semi-circular canals, while the fine adjustment is effected through a combination of muscle sense and plantar reflex.

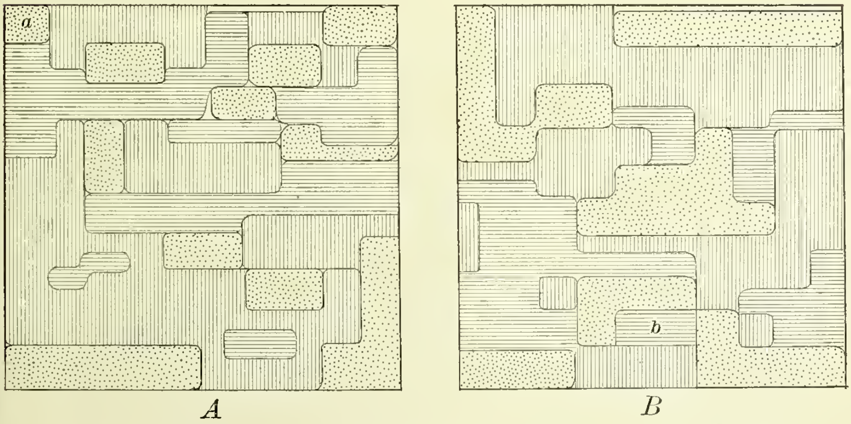
Besides the important part which the muscle-sense plays in the maintenance of equilibrium it serves the organism *in adjusting all motor activities to the required conditions.* The consciousness of a certain amount of tension upon muscles or tendons seems to be the thing which governs the amount of energy liberated in the muscle to accomplish a subsequent similar act. Every one has experienced the surprise and awkwardness in coördination which is likely to occur when in a flight of stairs one step is much lower than the others. The usual energy and space adjustment has been ordered in the central nervous system in response to previous muscular sense. The new conditions take the nerve-muscle system by surprise. This is not the case when the vision supplements the other equilibration apparatus. If one sees an unusual step he voluntarily modifies the course of the reflexes.

The following tests were made upon a number of medical students to determine the acuteness of their muscular sense: (1) Two clamp-holders differing from each other in weight by eight per cent. were handed in turn to each student and were alternately lifted by both right and left hands. The determination made by each student was recorded without communication with others in order that the judgment of one should not influence that of another. Results: There were sixteen answers; twelve were correct as to which was heavier. The average per cent. of excess of weight estimated for the heavier object was 7.6 per cent., maximum fifteen per cent., minimum three per cent. (II) Two bottles differing from each other by eight per cent. in weight were similarly tested by a number of students with the following results: There were nineteen answers, of which eighteen were correct as to which object was the heavier. The average per cent. of excess of weight estimated for the heavier object by the eighteen correct answers was 11.7 per cent., the maximum being twenty-five per cent. and the minimum two per cent. The results of these two tests make it evident that the muscular sense is less acute than the tactile sense. In common with other senses it may be much improved by practice. Produce dealers can by experience estimate with astonishing accuracy a particular weight of any commodity.

III. THE TEMPERATURE SENSE.

The sense of temperature is a very unreliable index of the actual temperature of any substance because the cutaneous surfaces yield us only relative ideas. We can say whether or not a substance is warmer or cooler than the skin, but we cannot say how many degrees of temperature it has. Knowing the probable temperature of the skin one can, by practice, usually guess approximately what the temperature is; but at best the determination is based upon a series of judgments all of them subject to considerable error.

Fig. 224.



Two maps showing areas of temperature sense. The maps each represent an area of one sq. in. on the back of the left hand of Mr. A and of Mr. B. The axis of the limb is from right to left, or horizontal, as the figure stands. The "hot" spots are shaded horizontally: the "cold" spots vertically. The areas especially endowed with tactile sense are dotted. The tactile spot *a* measures $\frac{1}{100}$ sq. in.; the "hot" spot *b* measures $\frac{2}{100}$ sq. in.

Not all portions of the surface of the skin are able to yield temperature sensations and not all portions so endowed yield sensations of both heat and cold; but one small area responds to cold, one to heat, and another to neither. The areas which do not respond to heat or cold are not insensible, they are endowed with the tactile sense. All portions of the skin are sensitive to pressure stimuli; but most persons seem to be more sensitive to very light pressure stimuli upon the tactile areas than upon the temperature areas (hot and cold spots): this may be an illusion due to the partial distraction of the attention by the sensation of cold or heat and pressure when an object touches a temperature area while there is no such distraction when the object touches a tactile area.

The accompanying maps show the distribution of these areas on particular surfaces and give a general idea of the relative sizes, shapes and areas of cold, hot and pressure spots. From these maps and many others the following conclusions have been drawn:

(*a*) Certain areas of the skin are functionally differentiated to receive stimuli from objects warmer than the skin, certain areas to receive stimuli from objects colder than the skin.

(*b*) Homologous areas on different individuals are different from each other as to distribution of the cold and heat areas.

(*c*) The total area sensitive to cold is much greater than the total area sensitive to heat. If a piece of cold metal one inch square were laid upon the surface mapped from Mr. A's hand it would stimulate 49.5 cold-areas and 27 pressure-areas, or a total of 76.5 areas. If a piece of warm metal be applied to the same area it would stimulate 23.5 heat-areas and 27 pressure-areas = 50.5. This may account for the illusion that when two pieces having the same weight, one being cold and the other warm are laid upon contiguous areas the cold one will seem to be heavier than the warm one.

(*d*) As a rule the longitudinal axis of an area corresponds to the longitudinal axis of the part (arm or leg) examined.

(*e*) Symmetrically located areas on the same individual vary considerably in their distribution of heat, cold and pressure sensibility.

(*f*) Special areas,—*i. e.*, heat-areas or cold-areas,—are smaller on individuals showing greater sensibility in the æsthesiometer experiments.

(*g*) Certain small areas seem to be sensitive to neither pressure, heat, nor cold when the stimuli are moderate.

(*h*) A test-point, though varying only slightly in temperature, may, at one location, feel cool, on another cold, and on a third very cold.

(*j*) On the palm of the hand the points specialized in sensibility to heat or cold were smaller and fewer than in the same area on the back of the hand.

(*k*) A cold penny placed on the palm of the hand feels much smaller than when placed on the back of the hand.

B. THE SPECIAL SENSES.

An organ of special sense involves: (I) a sensory end-organ limited in location and specialized in structure; (II) an afferent conducting path which differs in no way histologically from other axis-cylinders, though it corresponds to a dendrite of the neuron histogenetically; (III) a brain-center which is a portion of the general sensorium; (IV) inter-central conducting paths between the sensorium and higher cerebral centers.

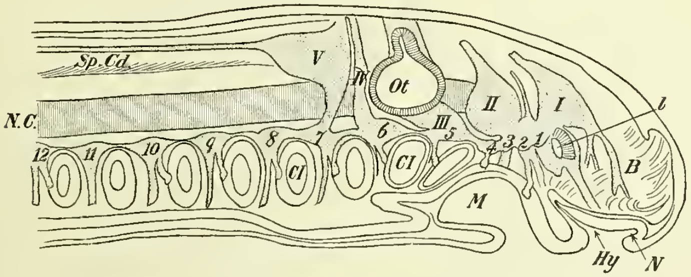
An act of special sensation involves: (I) special *stimulation* of the end-organ; (II) *transmission* to the sensorium; (III) *sensation*, or consciousness of the stimulation; these steps usually lead to the following: (IV) *perception* of the stimulating object; (V) *conception* of the object in its relation to other objects.

The *special sensations* include seeing, hearing, smelling, tasting, or vision, audition, olfaction, and the gustatory sense.

The researches of Kupffer ("*Cephalic Nerves*," *Verh. Anat. Ges.*, München, V., 22) and Froriep ("*Sense Organs*," *Arch. f. Anatomie*, 1886) show the origin of the organs of special sense from primitive structures in the lower vertebrates.

Fig. 225 is a reproduction of Kupffer's figure of the branchial sense organs of the larval cyclostome,—petromyzon. Note in the figure the five cephalic ganglia: I, ciliary ganglion; II, trigeminus; III, acustico-facial; IV, glosso-pharyngeal; V, vagus, which is continuous with the lateral nerve. Note the chain of epibranchial ganglia from 1 to 12; the anterior four being much crowded together, the last eight being evidently segmental, the 5th, 6th, and 7th corresponding definitely with the III, IV, and V cephalic ganglia respectively. Note also the brain (*Br.*), spinal

FIG. 225.



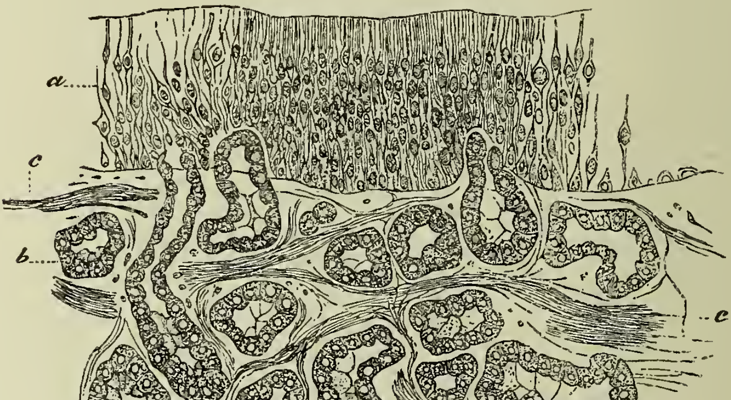
Larval petromyzon showing branchial sensory ganglia. (EDINGER after KUPFFER.)

cord (*Sp. Cd.*), lens of the eye (*l*), the nasal pit (*n*), the hypophysis or preoral pit (*Hy*), mouth (*M*), the gill clefts (*Cl*), the otocyst (*Ot*), and the notocord (*N. C.*).

Kupffer says regarding the development of sense organs: "There can be little doubt that the lateral ganglia (cephalic ganglia) and their sense organs as one series and the epibranchial ganglia and their sense-organs as another series *are common to all vertebrates*. It seems *certain* that the ear, *probable* that the olfactory organ and possible that the eye all belong to the lateral series."

Froriep discovered a series of rudimentary sense-organs associated with the epibranchial ganglia. They are now generally known as branchial sense-organs. Minot (1892) believed it probable that further investigation would "*demonstrate the existence of both series in the embryos of all vertebrates.*" Edinger, writing in 1896, cited recent literature showing that the probability of 1892 has become practically a certainty. We are, then, justified in looking upon the mammalian ear as a highly specialized product of evolution of one pair of a long series of lateral sense-organs. In the higher vertebrates the other lateral sense-organs are either specialized in other directions (eye, olfactory organ), are rudimentary in the adult, are rudimentary and transitory in the embryo, or, finally, wholly wanting even in the embryo.

FIG. 226.



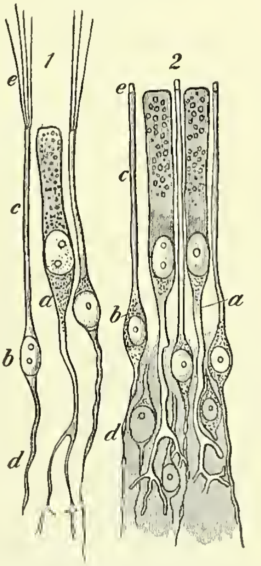
Section of olfactory mucous membrane.

IV. THE SENSE OF SMELL.

1. STRUCTURE OF THE OLFACTORY ORGANS.

The end-organ of smell may be described as the *regio olfactoria*, or upper part of the nasal passage, embracing the whole surface of the upper, with the upper part of the middle turbinated bone, also the upper one-third of the nasal septum. This region is out of the direct line of respiration, and all of the lower region or all of the nasal passage not included in the above enumeration is called the *regio respiratoria.* The regio olfactoria is so constructed as to present a very large surface to the air which passes through it. The mucous membrane of the olfactory region has a very thick, spongy corium in which are located the mucus-secreting glands of Bowman; and through which pass the fibers or fiber-bundles of the olfactory nerves, on their way to the cribriform plate of the ethmoid bone. (See Fig. 226.) The epithelium (See Fig. 227) consists of two kinds of cells. The epithelium proper or the supporting cells occupy most of the surface and extend to the corium by branching proximal ends. Between the supporting cells lie the olfactory cells or the *fila olfactoria.* The bodies of these cells lie deep in epithelial layer, and there is a thin, rod-like extension passing out to the surface of the epithelium distally, while the proximal extension is really a naked axis cylinder which, joining several of its fellows, passes as a non-medullate nerve into the olfactory bulb which lies above the cribriform plate. The interesting morphological feature shown here is in the homology between the olfactory cells and the cells of the spinal ganglia. The distal, protoplasmic extension of the olfactory cell is the afferent cell-branch or the *dendrite,* while the proximal, protoplasmic extension is the efferent cell-branch or the neurite or neuraxon, here modified into a naked axis-cylinder. This cell is a neuron of the I order.

FIG. 227.



Cells and terminal nerve-fibers of the olfactory region. (Highly magnified.) 1, from the frog; 2, from man; *a,* epithelial cell, extending deeply into a ramified process; *b,* olfactory cells; *c,* their peripheral rods; *e,* their extremities, seen in 1 to be prolonged into fine hairs; *d,* their central filaments. (SCHAEFER after SCHULTZE.)

This neuraxon undergoes arborization in the olfactory glomeruli, where they are in communication with the dendrites of the mitral cells of the olfactory bulb. (See accompanying Fig. 228.)

2. PHYSIOLOGY OF THE SENSE OF SMELL.

Olfactory sensation may be stimulated by gaseous or volatile substances, the requisite conditions seem to be that the matter shall be finely divided and diffused through the air. The act of inhalation carries a direct current of the odor-laden air along the regio respiratoria, but it diffuses readily into the regio olfactoria. To aid this diffusion most mammals intuitively "sniff" when

Fig. 228.

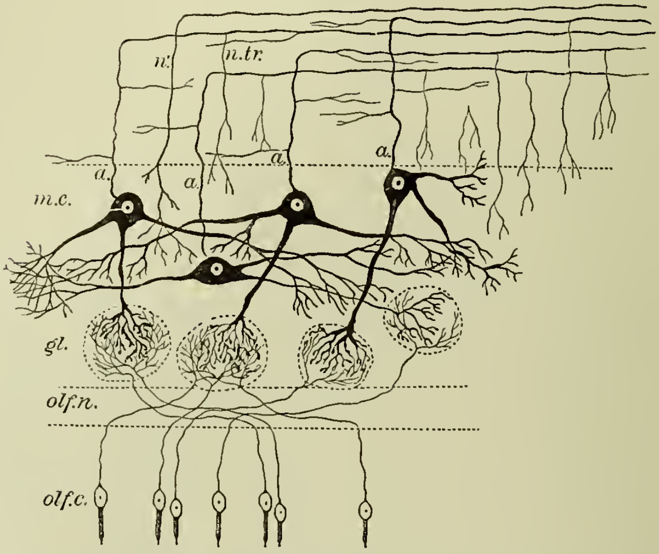


Diagram to show the relations of cells and fibers in the olfactory bulb. *olf.c.*, olfactory cells of M. Schultze in the olfactory mucous membrane, sending their basal processes as non-medullated nerve-fibers into the deepest layer of the olfactory bulb (*olf.n.*); *gl.*, olfactory glomeruli containing the terminal arborizations of the olfactory fibers and of processes from the mitral cells; *m*, mitral cells, sending processes down to the olfactory glomeruli, others laterally to end in free ramification in the nerve-cell layer, and their axis-cylinder processes, *a*, *a*, upwards, to turn sharply backwards and become fibers of the olfactory tract (*tr. olf.*). Numerous collaterals are seen curving off from these fibers; *n′*, a nerve-fiber of the olfactory tract apparently ending in a free ramification in the olfactory bulb. (Schaefer.)

they wish to "scent" an object. The sniffing consists in a series of quick inspirations. The rarefaction of the air in the olfactory region incident to the sniffing facilitates rapid diffusion of the odor-laden air into that region.

The stimulation of the olfactory cells by the odoriferous substance can take place only through *direct contact* of the substance with the cells. To this end the substance passes into solution in the film of moisture which covers the epithelial surface. The stimulating substance is in solution when the stimulation takes place. The sense of smell is much impaired or even suspended if the olfactory epithelium should become dry from any cause. On the other hand, odoriferous substances in solution in water do not stimulate the sense of smell when the water fills the nose. The water impairs the sensibility of the olfactory cells. But if an odoriferous substance in solution in normal saline solution be brought into contact with the olfactory epithelium the olfactory cells respond to the stimulus.

The *intensity* of the sensation varies with: (I) The area of the olfactory surface; (II) the concentration of the odoriferous substance; and (III) the frequency of conduction of the vapor to the olfactory region (the frequency of the "sniffs"). (Landois.)

The *acuteness* of the sense of smell varies with: (I) The size of the olfactory area; and (II) practice.

All attempts at a satisfactory *classification of odors* have failed. The French chemist, Septimus Piesse, arranged a scale of odors which he called the "*Odophone*"; but it was too arbitrary to be accepted.

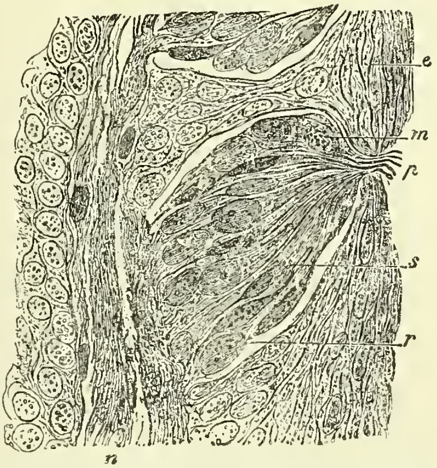
The *use of the sense of smell* to the system is primarily as a means of protection, warning the animal against the introduction of noxious foods, air or drinks into the system. Secondarily it is cultivated by some of the human family as a means of sense-gratification—of sensual gratification. Next to the seeking of pleasurable tactile sensations, it is the lowest form of sensuality.

V. THE SENSE OF TASTE.

1. STRUCTURE OF THE GUSTATORY ORGANS.

The tongue serves the function under consideration, but that organ serves also other functions, *e. g.*, mastication, deglutition, and articulation of speech. The tongue is not the specialized end-organ of taste. The specialized organ is the *taste-bud*. (Fig. 229.) Numerous taste-buds may be found in the epithelium of the oral mucous membrane. The accompanying figure (Fig. 230) shows that the taste-bud is an epithelial structure; *i. e.*, that it is a group of modified epithelial cells. The pavement epithelium of the oral mucous membrane is not adapted to the ready absorption of liquid. The bundle of spindle-shaped cells presenting their ends at the surface of the general epithelium is well adapted to the ready absorption of liquid, and this absorption of liquid seems to be an important part of the special function of the taste-buds. The accompanying diagram

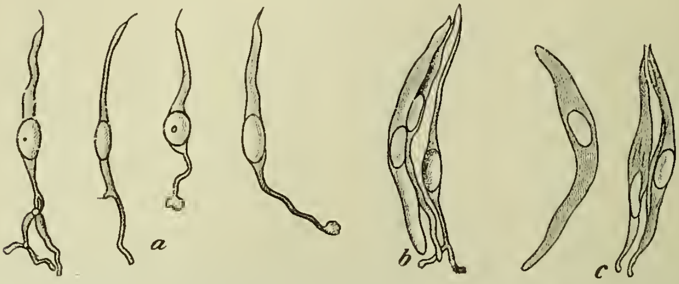
FIG. 229.



Section through the middle of a taste-bud. *p*, gustatory pore; *s*, gustatory cell; *r*, sustentacular cell; *m*, lymph cell, containing fatty granules; *e*, superficial cells of the stratified epithelium; *n*, nerve-fibers. (RANVIER.)

(Fig. 231) makes it evident that liquid absorbed from the surface (*s*) of the epithelium will pass, by capillary attraction, between the spindle-shaped gustatory cells and be brought into intimate contact with the filamentous ends of the gustatory nerve.

FIG. 230.



Various cells from taste-bud of rabbit. (600 diameters.) *a*, four gustatory cells from central part; *b*, two sustentacular cells, and one gustatory cell, in connection; *c*, three sustentacular cells. (ENGELMANN.)

If the liquid be an aqueous solution of some substance capable of stimulating the sensation of taste, the effect of the stimulation will be propagated along the afferent dendrite to the cell-body of the neuron, which lies in the ganglion of the nerve trunk, thence through the neuraxon to the central nervous system, within which a neuron of the second order transmits it to the sensorium. There has been much controversy as to whether the gustatory nerve-fibers are all contained in the glosso-pharyngeal trunk, or whether some of them may not reach the oral mucous membrane through the lingual branch of the trigeminus. Both nerves undoubtedly contain gustatory fibers. The gustatory fibers may readily pass from one trunk to another in the tympanic plexus, a condition which is

FIG. 231.

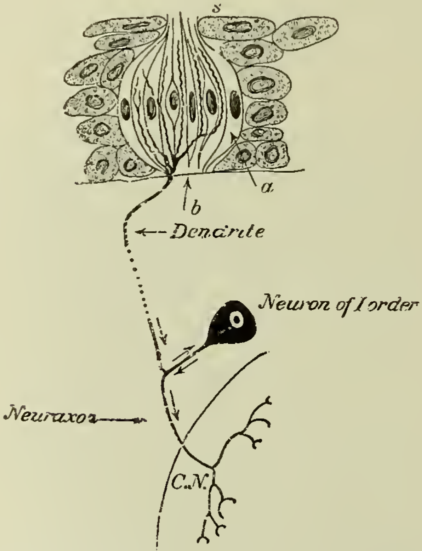


Diagram of taste-bud with gustatory nerve. Note that the epithelial cells which compose the taste-bud are broad encasing cells, (*a*) or slender gustatory cells. (*b*) Note the afferent dendrite arborizing among the gustatory cells and the afferent neuraxon passing into the central nervous system (*C.N.*) where it comes into relation with neurons of the II order. The cell body is located in the trunk-ganglion of the nerve of taste. (QUAIN after RETZIUS.)

known to exist in the case of the secretory and vaso-dilator fibers of the salivary glands (*quid vide*). There is probably one source for the gustatory nerve-fibers, and that source is probably the trunk (petrous) ganglion of the glosso-pharyngeal nerve.

The taste-buds are distributed (I) over the lateral surfaces of the circumvallate papillæ; (II) upon the fungiform papillæ; (III) upon the papillæ of soft palate, uvula, anterior pillars of the fauces, and surface of epiglottis.

2. PHYSIOLOGY OF THE SENSE OF TASTE.

a. A Summary of the Facts Concerning Taste.

Many of the perceptions attributed to taste really depend quite as much upon smell as upon taste. We usually apply the term *flavor* to those sensations which depend upon both smell and taste; *e. g.*, one speaks of the flavor of roast beef or of coffee. The fact that closure of the nose impairs the flavor of the beef or coffee, indicates that a part of the flavor is to be attributed to the sense of smell. The sense of taste alone seems to be confined to sensation arising from four distinct stimuli: (I) *sweet;* (II) *bitter;* (III) *acid;* (IV) *salt.* All purely taste sensations are either modifications of or combinations of these four fundamental sensations. The sense of taste may be excited only by those substances which pass into solution; *i. e.*, insoluble substances are tasteless.

The sensation will vary in strength with: (I) the *size of the area stimulated*, being more intense the greater the area stimulated; (II) the *concentration of the solution*, being more intense the stronger the solution; (III) the *temperature of the solution*, being more intense the nearer the temperature is to that of the blood; (IV) the mechanical friction of the tongue against the palate, being stronger with moderate friction than without it.

The sense of taste varies in acuteness: (I) through certain hereditary influences; and (II) through cultivation. A good example of marked acuteness of taste acquired by cultivation, may be found in the professional tea-tasters, and wine-tasters.

b. Practical Tests of the Sense of Taste.

1. To Determine the Acuteness of Taste.—Make four standard solutions as follows: (I) *Sugar:* 1 gm. of dry saccharose in 100 c.c. distilled water. (II) *Quinine:* 1 centigramme in 1000 c.c. of distilled water. (III) *Acetic acid:* 1 gm. of glacial acetic acid in 1000 c.c. distilled water. (IV) *Salt:* 1 gm. of dry sodium chloride in 100 c.c. distilled water.

In the use of these solutions prepare the gustatory surfaces by thoroughly rinsing the mouth with distilled water, or with boiled water. Take a uniform quantity of the solution into the mouth at each observation. A convenient quantity is 4 c.c. or a common teaspoonful. Rinse the mouth before each new observation.

The following table gives results obtained by a number of observers. (The numbers indicate the number of parts of water to one of the substance to be tasted.)

Mr.	Sugar.	Quinine.	Acetic Acid.	Salt.
A.	700	1,000,000	7,000	425
B.	600	500,000	8,000	500
C.	—	250,000	4,400	—
D.	300	400,000	3,000	700
E.	700	—	4,000	400
F.	400	400,000	6,000	600
G.	333	400,000	6,000	—
H.	500	400,000	4,500	480
I.	500	450,000	6,000	325
J.	650	200,000	7,500	325
Av.	1 to 520	1 to 444,000	1 to 5640	1 to 469

Besides the results here recorded numerous data were furnished by other observers.

(*a*) This table and the supplementary data justify the following conclusions:

(α) The acuteness of taste for sugar varies from one part of pure cane sugar in 300 parts of water, to 1 in 708, with an average of 1 in 520.

(β) The acuteness of taste for salt varies from 1 in 325 to 1 in 700, with an average of 1 in 469.

(γ) The acuteness of taste for acetic acid varies from 1 in 3,000 to 1 in 8,000, or an average of 1 in 5,640.

(δ) The acuteness of taste for sulphate of quinine varies from 1 in 200,000 to 1 in 1,000,000, with an average of 1 in 444,000.

From these results it is evident: (I) that there is considerable individual variation; (II) that the taste is more acute for the less common stimuli of bitter and acid than for the more common stimuli of salt and sweet.

(*b*) Several students recorded a marked decrease in the acuteness after the use of tobacco.

(*c*) One student recorded a noticeable increase in the stimulation when the solutions were warmed from 20°C. to 40°C.

(*d*) One observer found that the tip and edge of the tongue were more acute than other parts of the tongue in *detecting slight differences in the strength of the solutions.*

(*e*) One observer, reporting a series of very careful experiments upon four individuals, three of whom are members of the same family and accustomed to the free use of salt and vinegar in their regular diet, concluded: That the fourth individual, not accustomed to the free use of salt and vinegar, has a greater sensitiveness for saline and sour substances than do the three individuals who are so accustomed.

(*f*) As to the interval of time between the application of the stimuli and the taste perception the observations seem to justify the following conclusions:

(*α*) The interval between stimulation and sensation (latent interval) varies inversely as the number of papillæ per unit area in the portion of the gustatory apparatus stimulated.

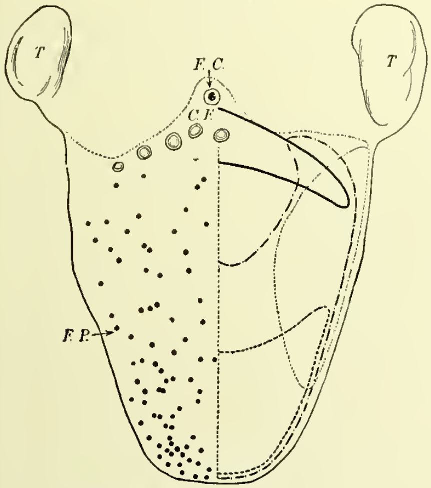
(*β*) The interval between stimulation and sensation varies directly as the blood-supply or blood-pressure of the part at the time of stimulation.

2. *To determine localization of the sense of taste, i. e.*, to find whether there are areas of gustatory region which are especially sensitive to particular stimuli; quinine, for example.

Solution: Through the aid of a probang or of a camel's-hair brush apply to different limited areas of the tongue, palate, fauces and buccal mucous surface either the standard solutions given above or somewhat stronger solutions of the same substances.

Results: The following figure (Fig. 232) gives the results which coincided substantially with those of other observers: Outline of tongue showing location of tonsils (*T*), foramen cæcum (*F. C.*), circumvallate papillæ (*C. P.*) and fungiform papillæ (*F. P.*) upon the left side, while the right side shows the outline of the area particularly sensitive to quinine (——) acid (. . . .), salt (— · —) and sugar (- - - -) respectively.

FIG. 232.



Localization of taste. Bitter, ——; acid, ...; salt, —·—·—; sweet, - - - -.

"Œhrwall has examined the different fungiform papillæ over the tongue with reference to their sensitiveness to taste-stimuli. One hundred and twenty-five separate papillæ were tested with succinic acid, quinine and sugar. Twenty-seven of the papillæ gave no response at all, indicating that they were devoid of taste fibers.[1]

Of the remaining ninety-eight, twelve perceived acid alone, three perceived sugar alone while none were found which reacted to quinine alone. The fact that some papillæ respond to only one form of taste sensation is evidence in favor of the view that there are separate nerve-fibers and endings for each fundamental sensation; but a majority of the papillæ (83) are provided with more than one variety of taste-fibers." (Henry Sewall, in *American Text-book of Physiology.*)

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[1] The 27 papillæ which gave no response to sour, sweet, of bitter, may have been sensitive to salt.

VI. HEARING.

INTRODUCTORY.

1. Physiological Acoustics.
2. Comparative Anatomy and Physiology of the Auditory Organ.
3. Embryology of the Auditory Organ in Vertebrates.
4. Summary of the Anatomy and Histology of the Ear.

THE PHYSIOLOGY OF HEARING.

1. The Transmission of Sound.
    a. *The Part Played by the External Ear.*
    b. *The Part Played by the Middle Ear.*
2. The Reception of Sound.
3. The Sensation and Perception of Sound.

VII. HEARING.

INTRODUCTORY.

1. PHYSIOLOGICAL ACOUSTICS.

a. Definitions.

(*a*) Acoustics is the Science of Sound, and comprises the study of sounds and of the vibrations of elastic bodies. Acoustics is concerned particularly with questions of the production, transmission and comparison of sounds.

(*b*) "Sound is always the result of rapid oscillations imparted to the molecules of elastic bodies, when the state of equilibrium of these bodies has been disturbed either by a shock or by friction." (Ganot.) Such bodies, always representing ponderable matter, tend to regain their position or condition of equilibrium only after performing on each side of that position very rapid vibratory movements the amplitude of which quickly decreases. The term *sound* is also applied to the sensation which these vibrations arouse in the brain.

(*c*) The term *physiological acoustics* may be applied to that portion of the general field of acoustics, which deals with the production, transmission and comparison of the sounds made by animals, or of the sounds serving as stimuli for animal sense-organs. Physiological acoustics deals, then, with the physical principles involved in the production of the voice; with speech, music, and the transmission of these sounds by the organs of hearing to the auditory nerve ends.

b. The Production of Sound.

That sound is produced by the vibration of elastic bodies may be readily confirmed by experiment. Ganot suggests the following experiment: Hold a bell-jar so that its axis is horizontal and its rim free. Tap it gently with a pencil; it emits a continuous musical sound. Lay any small body, like a piece of crayon or a nail, in the jar on its lower wall; hit the jar a smart rap; it emits a musical sound as before, and in the meantime is causing the free object within to jump about at a lively rate. The object is being struck at short intervals by the vibrating wall of the jar. In a similar manner a tuning fork or a violin string will throw off light objects which are placed upon it while it is emitting a sound. *Sound is produced by the vibration of elastic bodies. A musical sound or tone* is a regular continuous sound. *A noise* is an irregular discontinuous sound.

c. The Propagation of Sound.

Sound can be propagated only through the medium of ponderable matter, for if the air be withdrawn from the receiver of an air-pump a music-box in operation within the receiver, surrounded by the imponderable, luminiferous ether, can not be heard.

Sound is propagated through elastic, ponderable matter. All gases, liquids, and solids may transmit sounds. These bodies are acted upon by the vibrating source of the sound and are thrown into a series of waves which rapidly spread in all directions from the center of disturbance. In water-waves, or the undulations which sweep over the surface of a body of water, the individual molecules rise and fall, describing an ellipse whose long axis is *transverse* to the direction of propagation. In sound-waves the molecules move to and fro in a line *parallel* to the direction of propagation. This leads to *a series of alternating condensations and rarefactions of the medium.*

1. **Velocity of Propagation of Sound.**—(*a*) IN GASES.—Newton determined that the velocity of the propagation of sound in gases *is directly as the square root of the elasticity of the gas, and inversely as the square root of its density* $\left(v = \sqrt{\frac{e}{\partial}}\right)$. This formula with modifications for temperature, and barometric pressure yields the following results: velocity of sound in carbon dioxide, 856 ft. per sec.; oxygen, 1040 ft.; air, 1093 ft.; hydrogen, 4063.

(*b*) In Liquids.—The same general formula $\left(v = \sqrt{\frac{e}{\delta}}\right)$ as given for gases applied with modifications for liquids. The coefficient of elasticity (*e*) is very high for liquids, and though the density (*d*) is also great the high elasticity makes the velocity of sound in liquids much higher than it is in gases. For water the velocity is 4708 ft. at 80° C. to 5013 ft. per sec. at 30° C.; for absolute alcohol, 3854 ft. per sec. at 23° C.; for a solution of NaCl, 5132 ft. per sec. at 18° C.

(*c*) In Solids. The velocity in feet per second in caoutchouc, 197 ft.; in lead, 4030 ft.; in copper, 11,666 ft.; in steel wire, 15,470 ft.

2. **Reflection and Refraction of Sound.**—The echo, familiar to every youth, is a simple reflection of sound. The reflection of sound is subject to the following laws: (I) *The angle of reflection of sound is equal to the angle of refraction.* (II) *The incident sonorous ray and the reflected ray are in the same plane perpendicular to the reflecting surface.*

A *sound-lens* made of two circular sheets of collodion cemented together at their edges and inflated with CO_2 will bring sound waves to a focus. The ticking of a watch held beyond the principal focus of such a lens may be clearly heard in the conjugate focus of the lens though the conjugate focal distance may be many feet.

d. The Properties of Sound.

One sound may vary from another in intensity or loudness, in pitch and in quality.

1. **Intensity.**—(*a*) The intensity of sound varies inversely as the square of the distance of the sonorous body from the ear.

$$\left(I \text{ varies as } \frac{1}{D^2}\right).$$

(*b*) The intensity of sound increases with the amplitude of the vibrations of the sonorous body.

(*c*) The intensity of sound depends on the density of the air through which the sound is propagated.

(*d*) The intensity of sound is modified by the motion of the atmosphere, *i. e.*, by the wind.

(*e*) The intensity of sound is increased by the proximity of a sonorous body. (*e. g.*, The sounding box of a violin intensifies the sound produced by the vibration of the strings.)

2. **Pitch.**—The expression, "pitch of a sound," refers to the number of vibrations of the sonorous body in a unit of time. The greater the number of vibrations per second the *higher* the

pitch; the fewer the vibrations the *lower* the pitch. The number of vibrations which a sonorous body will make in a second depends upon several variable factors. In physiological acoustics we are interested particularly in the vibrations of strings and of membranes because the human voice is the sound of the vibrating strings—*the vocal cords*—and the hearing of the human voice and other sounds depends upon the vibration of a stretched membrane, *the membrana tympani.*

(*a*) THE PITCH OF A VIBRATING STRING.—"The vibration of a string stretched between two points depends upon the reflection, at either end, of the wave motion transmitted along the string. If a succession of waves travel along the string each wave will in turn be reflected at one end and travel back along the string, to be reflected again at the other end. The motion of any point of the string is, accordingly, the resultant of the motions due to waves travelling in both directions. If a string is to remain in a state of vibration it follows that the modes of vibration must be such that *the distance between the two ends* (the fixed points or terminal nodes) *contains an integral multiple of half the length of a wave*" (Shaw) (*i. e.*, $l=\frac{a\lambda}{2}$, when l = the distance—length of string—a the integral multiple and λ the fundamental wave-length. For the fundamental pitch of a string $a = 1$; $l=\frac{\lambda}{2}$, and $\lambda = 2l$).

In seeking a general formula for the pitch of a vibrating string we must first find an expression for the velocity of the undulation which sweeps along such a string. The fundamental equation for the velocity of an undulation is $v = \lambda n$, *i. e.*, if n waves pass a fixed point in a second, and if each wave has a length λ from crest to crest (node to node in the string); then the velocity would be n times λ. But we are seeking the value of n in terms applicable to the conditions. Our fundamental equation for n is from the above ($v=\lambda n$):

$$\text{(I)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad n = \frac{v}{\lambda}.$$

We know the value of λ in terms of length of string when the string is giving its fundamental tone:

$$\text{(II)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad \lambda = 2l.$$

It remains to express v in terms of tension, etc., applicable to the string. "A wave of any length travels along a taut string with a velocity equal to the square root of the tension (in dynes) divided by the mass of a unit of its length expressed in grammes per centimeter." (Lord Rayleigh, *Sound*, Vol. I., Chap. I.)

$$(\text{III}) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \; v=\sqrt{\frac{\tau}{\mu}}$$

For the tension in dynes is equal to 981 × the weight in grammes: $\tau=981g$. μ or the mass of a unit of length expressed in grammes per centimeter is really the density multiplied by the volume. The volume of a unit length equals πr^2, representing the density or specific gravity by δ, then $\mu=\pi r^2\delta$.

$$(\text{IV}) \ldots\ldots\ldots\ldots\ldots \; v=\sqrt{\frac{981g}{\pi r^2\delta}}=\frac{1}{r}\sqrt{\frac{981g}{\pi\delta}}$$

Substituting in (I) the values of v and λ we have

$$(\text{V}) \ldots\ldots\ldots\ldots\ldots\ldots\ldots \; n=\frac{1}{2rl}\sqrt{\frac{981g}{\pi\delta}}$$

Equation (V) expresses the number of vibrations per second in terms of length, radius, tension (weight) and density. Expressed as a variable by dropping the constants:

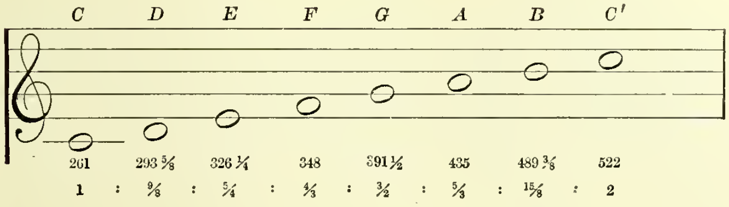
$$(\text{VI}) \ldots\ldots\ldots\ldots\ldots \; n \text{ varies as } \frac{1}{rl}\sqrt{\frac{g}{\delta}}$$

The verbal expression of the formula (VI) is: *The vibration frequency* (pitch) *of a string varies:* (I) *inversely as the radius;* (II) *inversely as the length;* (III) *directly as the square root of the tension in grammes;* (IV) *inversely as the square root of the density.*

(*b*) The Pitch of a Vibrating Membrane may be determined by the above formula (VI) under certain conditions: (I) The membrane must be circular (l), like a drum head; (II) the tension must be equal in all directions in the plane of a circle (g); (III) the thickness must be equal in all parts (r); (IV) the density must be equal in all parts. Once these conditions are filled we have in a vibrating membrane the equivalent of an infinite number of strings of equal length, tension, radius, and density, which will of course vibrate in unison, *i. e.*, the membrane will give the same fundamental tone as that given by a string representing a diameter of the membrane.

(*c*) The Musical Scale.—The standard pitch of an instrument is A which represents 435 vibrations per second; it is the middle A of the piano-forte. Note that the tone C' has just twice the number of vibrations of C. This relation holds good throughout the whole musical scale: A' has $(435\times 2=)$ 970 vibrations per second; while A—1 (one octave below middle A) has $(\frac{435}{2}=)$ $217\frac{1}{2}$ vibrations per second. The lowest C (C—3) of the piano has 32 + vibrations per second and the lowest C (C—4) of the pipe organ has 16 + vibrations per second. C^{II} has 1044 vibrations per second; C^{III}, 2088; C^{IV}, 4176; C^{V}, 8352; C^{VI}, 16704; C^{VII}, 33408.

FIG. 233.



3. **Quality.**—The variation in quality depends upon the combination of *harmonics* or *overtones*. The degree of complexity of a sound—the number of overtones present—together with the relative prominence or loudness of each overtone, is interpreted mentally as giving a distinctive *quality*, or *timbre*, or character to the sound heard. When one hears the A of a violin he not only recognizes the pitch and intensity, but he is able to say that it is produced by the violin. One does not consciously hear the harmonics or overtones as a rule; he hears only the fundamental tone *of a certain quality*. The flute gives practically a pure fundamental tone without any overtones. With a series of flutes which produce notes whose frequencies are in the ratios: 1:2:3:4:5, so mounted in a wind apparatus that they may be made to sound with a loudness which can be separately regulated, one can *build up any quality of sound*. Thus the infinite variety of sounds one hears in nature is very simply explained. Even the different vowel sounds depend for their differences upon the *modification in quality of a fundamental laryngeal tone*—given a particular quality by resonance of the organs of articulation—pharyngeal, oral and nasal cavities (*Medical Physics*, Daniell).

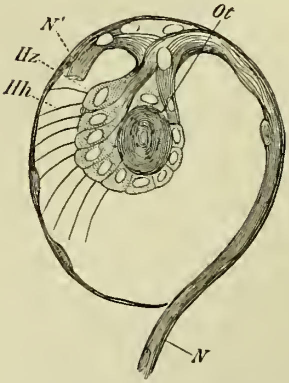
2. COMPARATIVE ANATOMY AND PHYSIOLOGY OF THE AUDITORY ORGANS.

There is no reason to believe that any of the Protozoa are sensitive to atmospheric vibrations. If they respond to the audible vibrations of the liquid media in which they rest, it is probable that these vibrations are really mechanical stimuli for their light unicellular bodies.

Some Cœlenterata possess auditory vesicles lined with epithelial cells, provided with bristle-like cilia, an otolith, and innervated by a nerve. Fig. 234 shows a section through such a simple auditory organ:

Among the *Echinodermata* only deep-sea holothurians, *Elasipoda*, possess auditory vesicles (56 in number). These are located along the course of the nerve cords and possess numerous otoliths.

Fig. 234.



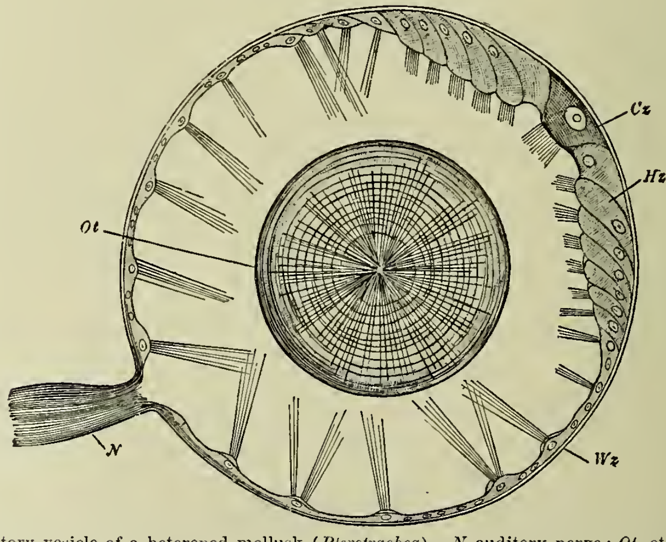
Auditory vesicle of a jelly-fish inclosing fluid provided with one or more otoliths. *N*, nerve; *Ot*, otolith; *Hz*, auditory cells with hairs, *Hh*. (Mills after Claus.)

The *Vermes*, as represented by the common earthworm, *Lumbricus*, though externally sensitive to the vibrations of the solids upon which they rest, are quite insensible to vibrations of the air. The microscope reveals no auditory vesicle in the earthworm.

The auditory vesicles of the *mollusca* are constructed upon the same general plan as those of the medusa. Fig. 235 shows Claus's section of the auditory vesicle of a heteropod mollusk. In most Lamellibranchs and Gasteropods and in the nautilus the auditory vesicles are innervated from the pedal ganglia.

The *Arthropoda* have more highly developed external ears than can be found elsewhere among the invertebrates. The crustacea as represented by the crayfish has auditory organs at the base of the antennules. "Here the auditory sac is permanently open,

Fig. 235.

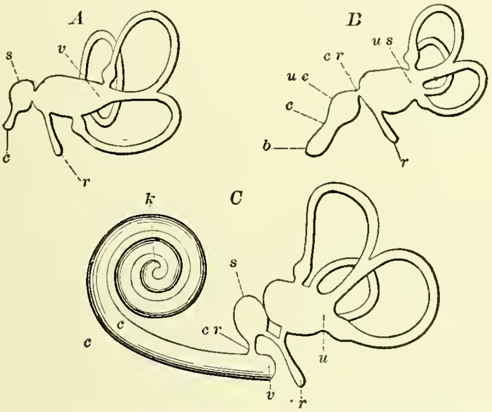


Auditory vesicle of a heteropod mollusk (*Pterotrachea*). *N*, auditory nerve; *Ot*, otolith in fluid of vesicle; *Wz*, ciliated cells on inner wall of vesicle; *Hz*, auditory cells; *Cz*, central cells. (Mills after Claus.)

though protected by bristle-like setæ. Within this sac a part of the wall is raised up into a ridge and the cells that form it are provided with delicate setæ at their free end and with nerve fibers at their base within. The sac is filled with a gelatinous fluid containing minute otoliths. Vibrations of the external medium set the otoliths in motion ; these beat upon the setæ, and these setæ affect the cells on the acoustic ridges, which, in turn, stimulate the nerve fibers which are in direct communication with the brain." (Bell.) The grasshopper, representing the *Insecta*, has a tympanum. This is a modification of the chitinous integument and consists of a cavity across which a delicate chitin membrane is stretched ; held taut by a delicate rim which in turn is stretched by a number of small radial muscles attached externally. Within the tympanum is an auditory ridge homologous to that described above in the crayfish.

The *Vertebrata* show the ear in its highest development ; though the lowest of the vertebrates (Tunicata, Amphioxus, etc.) give evidence of a continuity of the development from lower invertebrate forms. In all animals,—invertebrate and vertebrate alike—that possess an auditory vesicle this is invaginated from the epiblast and the pore which originally communicated with the exterior may remain open throughout adult life.

FIG. 236.



Diagrams to show the relations of the auditory labyrinth in the vertebrate series. *A*, fish ; *B*, bird ; *C*, mammal ; *u*, utriculus, with the three semi-circular canals ; *s*, sacculus ; *c*, cochlea ; *r*, aquæductus vestibuli ; *b*, lagena ; *cr*, canalis reuniens. In *C*, *r* is seen to divide into separate passages for the utriculus and sacculus ; the vestibule is seen to have a cæcal sack at *v* ; *k*, coil of the cochlea. (After WALDEYER.)

All higher vertebrates possess an internal ear (modified auditory vesicle) of considerable complexity, showing a *vestibule* and a series of *semicircular canals.* The mammals possess in addition a complex structure called the *cochlea.* Waldeyer's figure (Fig.

236) shows the variations in the structure of the auditory vesicle in fishes, birds, and mammals. The embryology and the anatomy of the mammalian ear may be taken to represent the higher vertebrates.

3. EMBRYOLOGY OF THE AUDITORY ORGAN IN VERTEBRATES.

a. Comparative Embryology.

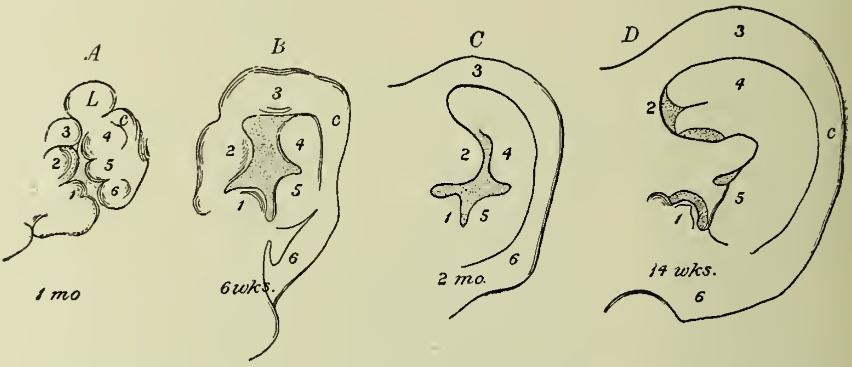
The origin of the ear from one of the lateral ganglia of the petromyzon, as maintained by Kupffer and now generally accepted has been discussed above. (See p. 458.)

The lowest mammals show a clear relation to the birds in the early steps of development; a relation which is not by any means effaced in the adult structure.

b. Special Embryology of the Human Ear.

1. **Development of the External Ear.**—The external meatus corresponds to the invaginated part of the branchial cleft and is therefore lined with epiblast. The pinna is developed (Fig. 237) from six eminences which surround the external end of the meatus. By the fourteenth week the form has already approximated that of the adult ear.

Fig. 237.



Development of the pinna. 1, tragus; 2, 3, *C*, Helix; 4, anthelix; 5, antitragus; 6, tænii lobaris. (Minot.)

Sometimes the pinna is arrested in its development. The small, round, thick ear, such as shown in *D*, is almost sure to be associated with a greater or less degree of arrest of psychical development.

2. **Development of the Middle Ear.**—For the details of the development of the middle ear, especially the bones of the middle

ear, see any work on the histogenesis of the pharynx. The following is a summary:

(I) The tympanic cavity and the Eustachian tube are developed from the first branchial pouch, hence called the "*tubo-tympanal pouch.*" It is lined with hypoblast.

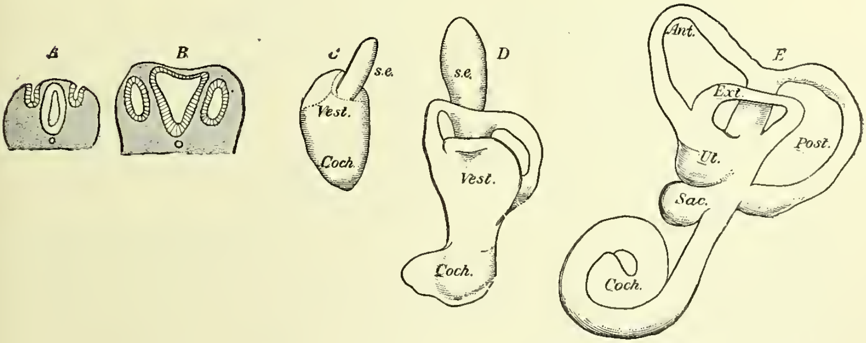
(II) The malleus is developed from a part, probably the cerato-branchial segment,—of the *1st branchial arch.*

(III) The incus is developed from a part,—probably epibranchial segment of the *1st branchial arch.*

(IV) The stapes is developed as an osseous deposit in the ligamentous connective tissue, connecting the fenestra ovalis with the incus. The hole in the stapes, which gives it its distinctive form, was occasioned originally by the presence of an artery, around which the ossification took place.

3. **The Development of the Labyrinth.**—*The Otocyst:* In the earliest stages of embryonic development when the anterior end of the neural tube has been definitely divided into primary fore-brain, mid-brain, and hind-brain vesicles, there appears on either side of the hind-brain vesicle a minute pit, which is invaginated from the epiblast and therefore lined with epiblast. This pit, the beginning otocyst, continues its invagination until it divides off from epiblast and begins a gradual migration through the delicate mesenchymal embryonic tissue toward its future position (see Fig. 238, *A* and *B*).

FIG. 238.



Development of the membranous labyrinth. Beginning of otocyst in the human embryo. *A*, 2.4 mm. in length; *B*, 4 mm. in length; *C*, otocyst of human embryo 4 weeks (HIS); *D*, human embryo 5 weeks (HIS); *E*, membranous labyrinth of 2 months embryo (HIS). (MINOT.)

In the meantime the otocyst rapidly enlarges and by the fourth week the saccus endolymphaticus (*s. e.*) is beginning its development (Fig. 238, *C*).

The third stage makes the development of the semicircular canals (Fig. 238, *D* and *E*). Note the order in which these are developed. Note also the development of the cochlea.

From this series of figures it is evident that the epithelial lining of the membranous labyrinth is epiblastic. At first composed of undifferentiated columnar cells there comes to be, in man, six areas within the membranous labyrinth where the epithelium is highly differentiated. Of these the most highly specialized is the organ of Corti, which undoubtedly represents the end-organ for the perception of sound. Besides the organ of Corti there is one specialized area in each semicircular canal. The *Crista acustica*, and one in the Utriculus, the *Macula acustica utriculi*.

4. SUMMARY OF THE ANATOMY AND HISTOLOGY OF THE EAR.

(*a*) The organ of hearing is divisible into (I) external, (II) middle, and (III) internal ear; or (I) pinna and meatus, (II) tympanum, and (III) labyrinth. (See Fig. 239.)

FIG. 239.

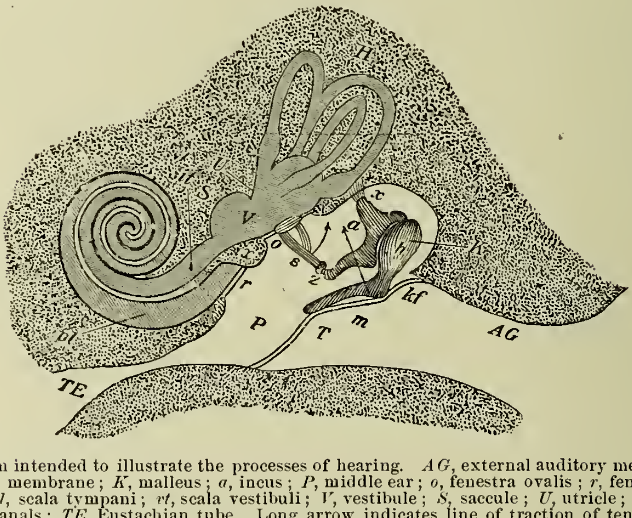


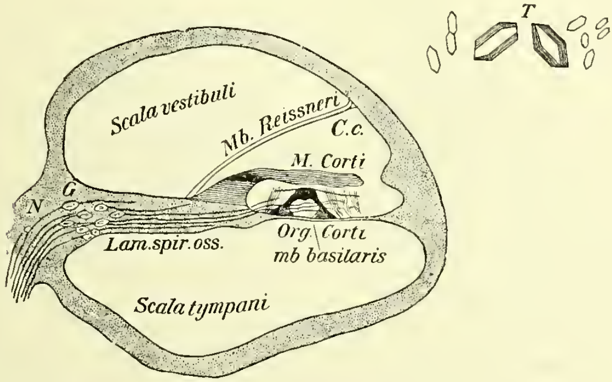
Diagram intended to illustrate the processes of hearing. *AG*, external auditory meatus; *T*, tympanic membrane; *K*, malleus; *a*, incus; *P*, middle ear; *o*, fenestra ovalis; *r*, fenestra rotunda; *pl*, scala tympani; *vt*, scala vestibuli; *V*, vestibule; *S*, saccule; *U*, utricle; *H*, semicircular canals; *TE*, Eustachian tube. Long arrow indicates line of traction of tensor tympani; short curved one that of Stapedius. (After LANDOIS.)

(*b*) The tympanum lies in a hollow in the petrous portion of the temporal bone. The tympanic membrane (*T*) cuts it off from direct connection with the external atmosphere. The Eustachian tube (*TE*) brings it into indirect connection with the air through the pharynx and external respiratory passages. The tympanum consists of a chain of bones: the malleus (*h*), the incus (*a*) and the stapes (*s*). The malleus is fastened to the membrana tympani and the stapes to the membrane which closes the foramen ovalis.

(*c*) The labyrinth lies within a cavity in the petrous portion of the temporal. The cavity with its various canals is called the *bony labyrinth.*

(*d*) Within the cavity of the bony labyrinth, but very much smaller than the cavity lies the *membranous labyrinth.* (See Figs. 236 and 238.) From the embryology it is evident that the epithelium of this membraneous labyrinth is epiblastic. Between this structure and the bony wall there is a considerable space occupied by two large lymph channels. The one above the epiblastic membranous labyrinth is the scala vestibuli, so called because it is continuous with the vestibule. The one below is called the scala tympani, which passes into the foramen rotundum separated from the tympanum by a thin but dense and strong membrane. Fig. 240 shows a cross-section of one whorl of the cochlea, with the membranous labyrinth, marked *C.c.* (Canalis cochlearis) and the large lymph spaces above and below.

Fig. 240.



Section of one whorl of cochlea.

(*e*) Note the little bony shelf (Lamina spiralis) which extends out from the inner wall of the bony canal and reaches about three-fifths of the way across to the outer wall, where there is a corresponding ridge. The space between the spiral lamina and the outer ridge is spanned by a dense membrane (membrana basilaris) which is composed in its $2\frac{1}{2}$ spiral turns of about 24,000 parallel, radial fibrillæ. The length of the fibrillæ which constitute the basilar membrane varies; *i. e.*, the width of the membrane varies in different parts of the cochlea:

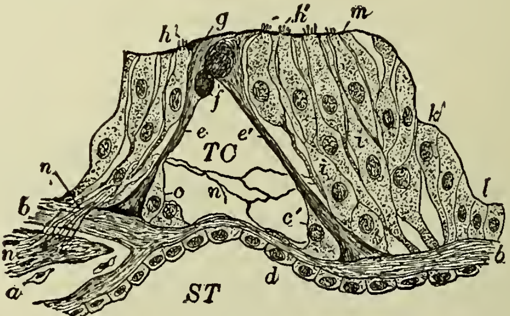
(I) At the beginning of the basal coil of the cochlea, 0.041 mm.
(II) Average for basal coil of cochlea, 0.21 mm.
(III) Average for middle coil of cochlea, 0.34 mm.
(IV) Average for apical coil, 0.36 mm.
(V) Length at end of apical turn, 0.495.

The longest fibrilla is 12 times the length of the shortest one.

(*f*) Between the basilar membrane and the membrane of Reissner is the epiblastic end-organ of hearing—the organ of Corti, whose general structure is indicated in Fig. 240.

(*g*) The Organ of Corti consists essentially of: (I) The rods or *pillars of Corti,* which are secured by the epiblastic cells *c* and *c'* (Fig. 241), and are chitinous in their general character. (II) The *inner and outer hair cells* so called from the short bristle-like hairs which extend from the upper ends. There are five rows of hair cells, one inner numbering about 3500 and four outer numbering about 12000. (III) The supporting cells or cells of Deiters. (IV) The reticular membrane, continuous with the outer ends of the rods of Corti and of the same sort of material as they. (V) The filamentous endings of the auditory nerve about the proximal ends of the hair cells.

FIG. 241.



Section of Corti's organ from guinea-pig's cochlea: *ST*, scala tympani; *TC*, tunnel of Corti; *a*, bony tissue of spiral lamina; *b*, fibrous tissue covering same continued as substantia propria of basilar membrane; *c*, *c'*, protoplasmic envelope of Corti's pillars (*e*, *e'*); *d*, endothelial plates; *f*, heads of pillars containing oval areas; *g*, head-plates of pillars; *h*, *h'*, inner and outer hair cells; *m*, membrana reticularis; *k*, *l*, cells of Henson and of Claudius; *n*, nerve-fibers; *i*, cells of Deiters. (PIERSOL.)

(*h*) There is an area of specialized innervated epithelium in the saccule and one in the utricle.

(*j*) The three specialized epithelial areas in the semicircular canals have been depicted and discussed under *Maintenance of Equilibrium* (q. v.).

(*k*) Fig. 240, *T,* shows some typical otoliths.

THE PHYSIOLOGY OF HEARING.

1. THE TRANSMISSION OF SOUND.

a. Part Played by the External Ear.

1. **The Pinna or Auricle.**—The part which it plays in man is so slight as to be practically disregarded. Abnormal projection of tragus over mouth of meatus obstructs sound waves.

2. **Meatus Externus.**—(*a*) THE CALIBRE is usually smallest at inner end near membrana tympani, though it is smaller in the middle (inner end of cartilaginous portion) than between that and the membrana tympani. If there is an abnormal narrowing of the inner segment there is no impairment of the hearing. If there is an abnormal narrowing of the outer end there is an unmistakable impairment of hearing.

(*b*) COURSE.—The meatus presents two segments meeting at an obtuse angle, the cartilaginous portion passes upwards and inwards and backwards, the bony portion passing downwards, forwards and inwards. This makes a direct transmission impossible; the sound waves must be reflected at least twice before impinging upon the membrana tympani.

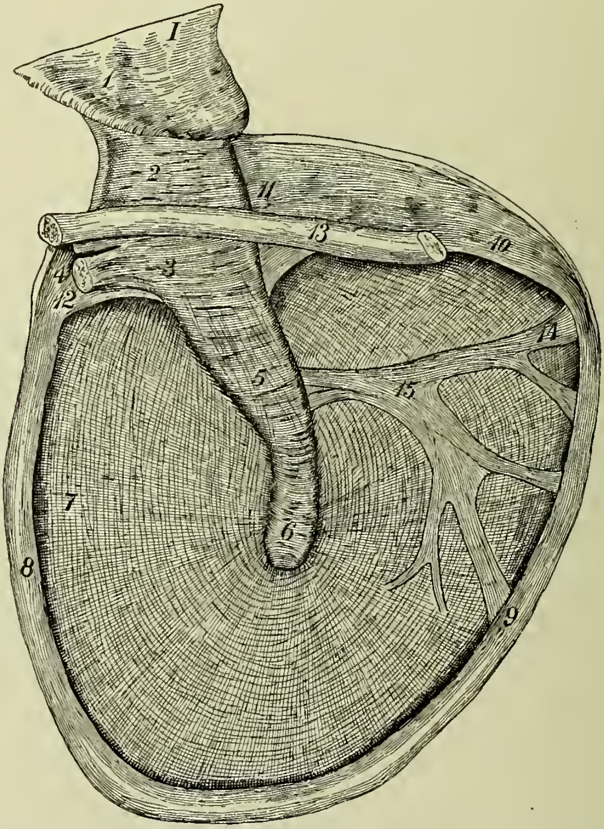
(*c*) REFLECTING SURFACES.—The description already given would lead us to suppose that these surfaces are conical ones, but the cross-section of the meatus is always elliptical in general outline and there is a depression on the *posterior* wall of the cartilaginous segment and one on the *anterior* wall of the bony segment. The more external depression presents an *ellipsoidal* surface, while the more internal one presents a *paraboloid* surface. Professor Dench in his text-book on the diseases of the ear cites this fact as advantageous but avoids telling what the advantages of a paraboloid surface are in this particular situation. Its advantages as a light reflector when the light is placed in the focus are familiar to every schoolboy. What are its advantages here?

(*d*) THE HAIRS AND SECRETIONS of the meatus are for protection.

3. **The Membrana Tympani.**—(*a*) General Structure: This delicate membrane possesses a *skin*, a mesenchymal *framework* and a hypoblastic *mucous membrane.* The mesenchyme consists of inelastic *connective tissue fibers which are either circular or radial.* The accompanying figure (Fig. 242) shows the general course of the radial and circular fibers of the middle layer or framework of the membrane.

(*b*) The *angle* at which the membrane tympani is set with respect to the axis of the bony segment of the meatus is not without importance. The lower half of the membrane inclines towards the axis of the meatus leaving an angle of about 55° and the upper half of the membrane inclines still more, leaving about 45° or less between membrane and axis. (See Fig. 243.)

Fig. 242.



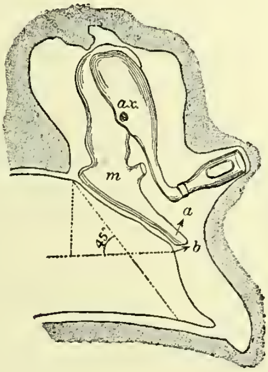
Photographic representation of right membrana tympani, viewed from within. 1, divided head of malleus; 2, neck; 3, handle, with attachment of tendon of tensor tympani; 4, divided tendon; 5, 6, long handle of malleus: 7, outer radiating and inner circular fibers of tympanic membrane; 8, fibrous ring encircling membrana tympani; 9, 14, 15, dentated fibers of Gruber; 10, 11, posterior pocket connecting with malleus; 12, anterior pocket; 13, chorda tympani nerve. (After Flint and Rüdinger.)

(c) *The Area of the Membrane:* It presents an elliptical surface whose axes are about 10 and 8 mm. The area would be approximately ($a=\pi r^2$; $a=3.1416\times(4.5)^2=$) 63.5 sq. mm.

(d) *The Question of Fundamental Tone*: Every fixed taut string and typical drum membrane possesses a fundamental tone. If the membrana tympani possessed a fundamental tone it would greatly impair its utility as a transmitting membrane for sounds of different pitch. The *membrana tympani does not* possess a fundamental tone because: (I) It is elliptical in outline. (II) Its vibrations are dampened by the attachment of the handle of the malleus. (III) The connective tissue fibers which radiate outward from the handle of the malleus as a part of the substantia propria of the membrane are of various lengths and of slightly varying tension. *A fundamental tone for the membrana tympani is therefore an acoustic impossibility.*

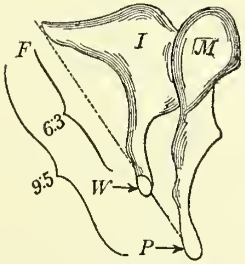
(*e*) *The external convexity of its radiating fibers:* Helmholtz has shown that an impulse against the convex surface of the taut membrane will have a greater effect in driving the handle of the malleus inward than would be the case if the taut membrane were a plane surface. When we consider, however, that the direction of this increased force would be as indicated by the arrow *a*, Fig. 243, instead of the direction of arrow *b* the required direction; the advantage is not so great as might first appear, being approximately two-fold, or the intensity is about doubled.

FIG. 243.



Showing incline of membrana tympani.

FIG. 244.



Lever system of the ear.

b. Part Played by the Middle Ear or Tympanum.

(*a*) *The Eustachian tube* permits equalization of pressure inside and outside of the cavity.

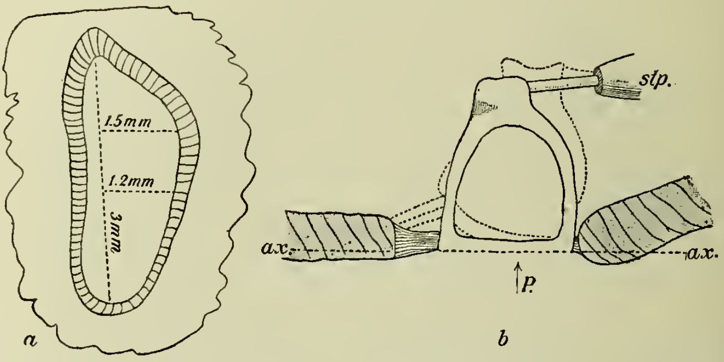
(*b*) *The lever system.*

(*α*) For the transmission of sound the malleo-incudal combination moves as one lever, while the stapes simply transmits the movements of the end of the incus to the oval window.

(*β*) For protection of the membrane which closes the oval window and to which the stapes is attached the malleo-incudal articulation is subject to motion in such a direction as to permit the handle of the malleus to be displaced outward without carrying the incus with it.

(γ) The lever arms (Fig. 244) have the ratio 6.3 mm. to 9.5 mm. The maximum movement of the end of the handle of the malleus is 0.097 mm., almost 1 mm. The distance traveled by the weight would be $= \frac{0.097 \times 6.3}{9.5} = .0643$ or a little more than $\frac{1}{16}$ of a mm. (Helmholtz). In the meantime the force has been augmented by the ratio $\frac{9.5}{6.3}$ or about 1.5 times. Summing it up: *the foot of the stapes vibrates through two-thirds the amplitude with 1½ times the force represented in the vibration of the malleus handle.*

FIG. 245.



Diagram, showing the shape and dimensions of the foot of the stapes (*a*), and the effect of contraction of the stapedius muscle (*stp.*), lifting the "toe" of the stapes up from the plane of the foramen (*ax*). (After TESTUT.)

(δ) The size of the foot of the stapes:
The area of the fenestra = 3.8 sq. mm.
The area of the foot is 2.65 sq. mm.
The area of the annular ligament is 1.15 sq. mm.

c. The Summed-up Force.

(α) As all of the energy received by 63.5 sq. mm. of tympanic membrane is transmitted to 2.65 sq. mm. of stapes we have a proportionally greater intensity of vibration.

(β) The convexity of the membrane increased the intensity. Assume a ratio of 2:1.

(γ) The lever system increases the intensity by a ratio of $\frac{9.5}{6.3}$. Summing up these ratios we have a final intensity (I) bearing the following ratio to the initial intensity (i):

$$\frac{I}{i} = \frac{63.5}{2.65} \times \frac{2}{1} \times \frac{9.5}{6.3} = 72.16.$$

The intensity per unit area is multiplied about 72 times in the course of its transmission. On the other hand, the amplitude is decreased to only $\frac{2}{3}$ of the original amplitude.

d. The Movements of the Stapes.

The full-line figure indicates the position of the stapes when the stapedius muscle (*stp*, Fig. 245) is relaxed. The dotted outline indicates the position of the stapes when the muscle is strongly contracted. This shows the motion of the stapes to be a rocking around the pivot, *p*. The wider area of the annular ligament anteriorly permits the motion. The maximum amplitude of the upper end of the stapes is about 0.064 mm. or $\frac{1}{16}$ mm. That would give the anterior end of the foot an amplitude considerably more than $\frac{1}{16}$ mm. and the posterior end or heel an amplitude of about zero or even possibly a slight negative vibration. But these are the conditions when the pitch is low, the amplitude of the membrana tympani great and the stapedius strongly contracted. These conditions would be likely to exist when the ear is receiving loud noises.

In the reception of the musical tones of the human voice or of a musical instrument it is not probable that the rocking motion exists. The amplitude of the motion may be as little as $\frac{1}{10000}$ mm.

e. The Perilymph of the Scala Vestibuli.

This takes up the vibrations of the foot of the stapes and transmits them to the organ of Corti, and through the scala tympani back to the foramen rotundum, whose membrane serves to equalize and temper the pressure within the labyrinth.

2. THE RECEPTION OF SOUND.

The end-organ of sensation is the organ of Corti. The modified epiblastic cells are the hair cells of the organ of Corti. About these modified epiblastic cells, or special receiving cells, the dendrites of the cochlear branch of the auditory nerve arborize. The cell body of the auditory neuron of the *I* order (whose dendrites arborize about the hair cells) lies in the spiral ganglion; the neuraxon, neurite or axon passes to the sensorium of the central nervous system. The way in which the terminal nerve ends are stimulated is a matter of speculation.

(*a*) Helmholtz's Theory briefly expressed is : 1st. The vibrations of the medium received by the membrana tympani are transmitted across the tympanic cavity and to the perilymph of the vestibule, with somewhat decreased amplitude, but much increased intensity, as given in detail above. 2d. The perilymph as well as the endolymph of various canals of the cochlea take up vibrations which correspond in number per second (pitch) with their own. 3d. The hair-cells resting upon fibrillæ which are set into vibration vibrate with the fibrillæ and thus stimulate the nerve filaments which arborize around them.

(*b*) The Telephone Theory of Waller.—Waller's theory makes the basilar membrane analogous to the telephone membrane which, as we know, may be thrown into vibrations of varying pitch, even reproducing a piece of music with its complex chords. The movements of the membrane here represent a resultant of all the impulses which affect it, and bodies resting upon such a membrane would likely be affected in a manner analogous to the way in which fine sand on a vibrating plate is affected; *i. e.*, throw into an infinite variety of resultant patterns or combinations. This theory makes perception of different tones a perception of different combinations.

3. THE SENSATION AND PERCEPTION OF SOUND.

a. The Range of Auditory Sensation and Perception.

1. **The Range of Pitch.**—(*a*) *The lower limit* is generally accepted as 16 vibrations per second.

(*b*) The upper limit is far beyond the upper note of the pianoforte, being usually somewhere in the octave between C^{VI} and C^{VII} above middle C, *i. e.*, representing between 16,704 and 33,408 vibrations per second. (International pitch.)

(*c*) *The range* would thus be for the human ear 10 to 11 octaves. The range for one particular human ear would probably not exceed 9 or 10 octaves, because an ear that can perceive 33,000 vibrations per second would not perceive 16 vibrations per second as a continuous musical tone, but as a rapid succession of noises. Nine octaves may be accepted as the average limit for the individual human ear.

(*d*) Problems:

(I) If the human ear can distinguish musical tones over a range of 9 octaves, how many fibrillæ of the basilar membrane would represent one tone?

(II) How many hair cells of the inner row would represent one tone?

(III) If the human perception is capable of distinguishing stimuli affecting two adjacent hair-cells, what fraction of a tone should be differentiated?[1]

The range of perception of pitch varies with age. At the age of ten years the upper limit of pitch is about 40,000 per second (E^{VII}), while at the age of fifty years it has receded to about 30,000 per second (B^{VI}).

---

[1] Weber says: "Accomplished musicians can appreciate differences in pitch as small as $\frac{1}{64}$ of a tone."

2. **The Range of Intensity.**—The lower limit of the range of intensity represents the acuteness of the hearing for faint sounds. Schafhäutl says: "A person of acute hearing can detect the sound made by a cork ball weighing one milligram (0.001 gm.) falling one millimeter (1 mm.) upon a glass plate 91 millimeters distant from the tip of the tragus and directly opposite to the meatus."

b. Judgments Based upon Auditory Sensations and Perceptions. Estimate of Distance and Direction of Source of Sounds.

This topic belongs to psychology. It may be briefly stated that the estimate of direction and distance is neither a sensation, a perception, nor a conception, but is the result of subconscious reasoning based upon a series of sensations, perceptions and conceptions. The young child estimates direction and distance only after many sensations have been received. With increasing experience the estimation of direction and distance becomes gradually more perfect. At first the result of a conscious effort it becomes eventually subconscious—really reflex.

VII. VISION.

INTRODUCTORY.

1. Physiological Optics.
2. Comparative Physiology of Vision.
3. Embryology of the Human Eye.
4. Summary of the Anatomy and Histology of the Eye.

THE PHYSIOLOGY OF VISION.

A. Visual Optics: The Eye as an Optical Instument.

1. Visual Refraction: The Refractive Apparatus of the Eye.
    - *a. Application of the Laws of Refraction to the Mammalian Eye.*
    - *b. Accommodation.*
        - (1) The Mechanism of Accommodation.
        - (2) The Range of Accommodation.
    - *c. Imperfections of the Refractive Apparatus of the Eye.*
2. Visual Mechanics: The Directive Apparatus of the Eye.
    - *a. Monocular Fixation.*
    - *b. Binocular Fixation and Convergence.*

B. Visual Sensation: The Eye as the Sense-organ of Vision.

1. Retinal Stimulation.
    - *a. The Stimuli.*
    - *b. The Irritability of the Retina.*
        - (1) Factors Involved in Retinal Irritability.
        - (2) Direct and Indirect Vision.

2. Visual Sensations.
    - *a. Fundamental Sensations.*
        - (1) Form.
        - (2) Intensity.
        - (3) Color.
    - *b. Secondary Sensations.*
        - (1) After-Images.
        - (2) Contrast.
    - *c. Color-Blindness.*
        - (1) Complete Color-Blindness.
        - (2) Yellow-Blue Blindness.
        - (3) Red-Green Blindness.
        - (4) Acquired.
        - (5) Normal Color-Blindness.
3. Visual Perceptions and Judgments.
    - *a. Acuteness of Vision.*
    - *b. Visual Estimates.*
        - (1) Estimate of Distance.
        - (2) Estimate of size.

VII. VISION.

INTRODUCTORY.

1. PHYSIOLOGICAL OPTICS.

a. Definitions.

(*a*) Optics *is the science of the phenomena of Light.* It comprises the study of the sources of light; the production of light; the propagation of light, and its various properties.

(*b*) Light is a Mode of Motion. The luminosity of a body is due to an infinitely rapid vibratory motion of its molecules, which, when communicated to the ether is propagated in all directions in the form of spherical waves, and this vibratory motion, transmitted to the retina, calls forth the sensation of vision. (Ganot.) The vibrations of the ether are transverse to the direction of the undulation—*i. e.*, they are *transversal vibrations.*

(*c*) A Luminous Ray is the direction of the line in which the light is propagated. Every luminous body emits divergent, rectilinear rays from all points of its surface, and in all directions.

(*d*) A Medium is any space or substance which light can traverse. Media may be transparent, or translucent.

Transparent media may be of various densities, glass is more dense than water, and water more dense than air, lower strata of air more dense than higher strata.

(*e*) The Term Physiological Optics may be applied to that portion of the general field of optics which deals with the transmission of light through the media of the organ of vision. Physiological optics deals properly with refraction, though reflection is also frequently treated under this head.

b. Refraction.

PROP. I. When a ray of light passes from one medium into another medium in a line perpendicular to the plane separating the two media, the ray will continue its course in an unbroken straight line in the second medium.

PROP. II. When a ray of light passes from one medium into another medium in a line not perpendicular to the plane separating the two media, the ray will be broken at the surface of the second medium.

FIG. 246.

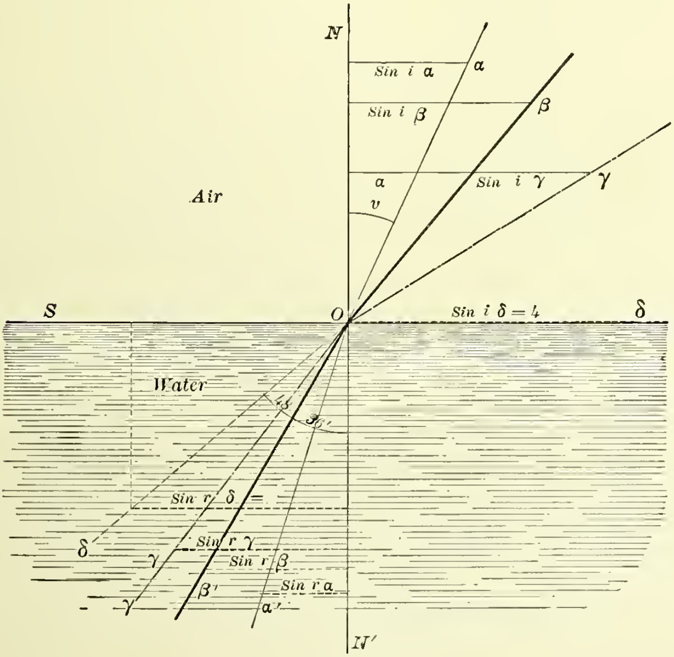


Diagram to illustrate refraction.

PROP. III. The plane determined by the two segments of the broken ray is perpendicular to the plane which separates the two media. *Corollary.* If the surface separating the two media be a curved one the plane determined by the ray will be perpendicular to a plane tangent to the curved surface at the point of intersection of the ray.

PROP. IV. If the second medium be denser than the first medium the angle between the ray and the normal will be less in the second medium than in the first and conversely.

PROP. V. The ratio between the sine of the angle of incidence and the sine of the angle of refraction is constant for any two media.[1]

$$\sin I : \sin R :: \sin i ; \sin r.$$

As $\frac{\sin I}{\sin R}$ is a constant for any particular medium it is customary to use μ to express this constant for air and each other medium respectively.

PROP. VI. If a ray pass from any medium through a denser medium which is bounded by two parallel planes, it emerges from the denser medium in a line parallel to its course before meeting that medium. (See Fig. 247.)

FIG. 247.

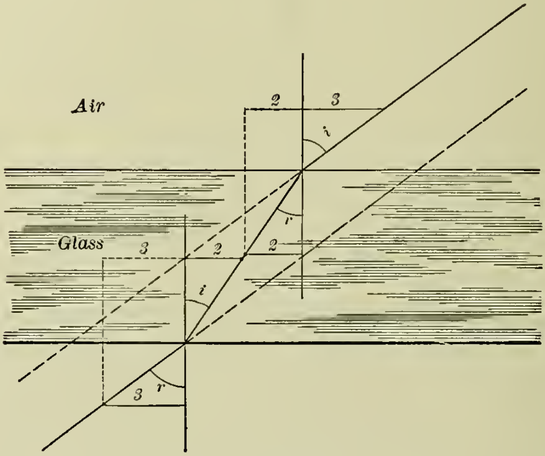


Diagram showing path of ray through a denser medium bounded by two parallel sides.

PROP. VII. If a ray pass from any medium through a denser medium which is not bounded by two parallel planes it emerges in a line not parallel to its original course but invariably refracted toward the base.[2] (See Fig. 248.)

---

[1] A *Normal* is a line perpendicular to the surface of a medium at the point of incidence. The *angle of incidence* is the angle between the incident ray and the normal (as $\angle a$). The *sine of the angle of incidence* in Fig. 246 is the line aN measured upon the radius aO. The *angle of refraction* is the angle between the refracted ray and the normal $\angle a'ON'$. The index of refraction of any medium is the ratio between the sine of the angle of refraction in that medium compared with the sine of the angle of incidence when light passes from *air* into the medium in question. For example, *index* of refraction for water $= \frac{\sin i}{\sin r} = \frac{4}{3} = 1.33$.

[2] "A *prism* in optics is any transparent medium comprised between two plane faces inclined to each other." (Ganot.) The *apex* of the prism is the line of intersection of the two planes. The *base* of the prism is the boundary surface opposite the apex, unless otherwise defined it is understood to be perpendicular to a plane bisecting the angle of the apex. The *angle* of the prism is the angle between the bounding planes. The *angle* of *deviation* is the angle between the *incident ray* and the *emergent ray.*

PROP. VIII. The rays of light emitted from a luminous point in the optical axis will, on passing through a convex lens, be converged toward the optical axis, *i. e.*, more convergent or less divergent.[1]

FIG. 248.

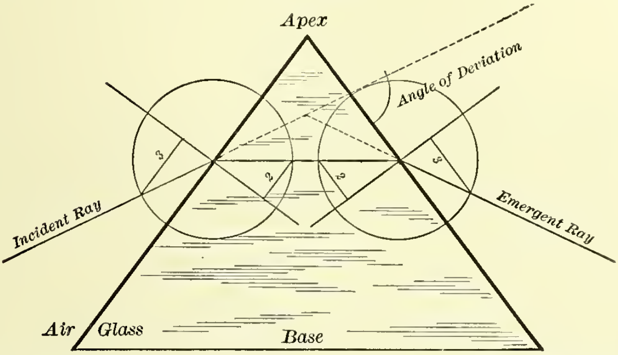


Diagram showing path of ray through a prism. Note that the incident ray is bent to the horizontal direction in the prism and is refracted again on emerging, still farther toward the base. If the two rays (incident and emergent) be extended in the dotted lines they will meet at an angle indicated in the figure. This angle is called the *angle of deviation.* (Wrongly indicated in the figure, unfortunately.)

[1] A *convex lens* is the optical equivalent of an infinite number of prisms standing base to base.

A *concave lens* is the optical equivalent of an infinite number of prisms standing apex to apex.

The *optical axis* is the line perpendicular to the plane of a lens and passing through its optical center.

The *optical center* is a point in the optical axis, any ray passing through which suffers no deviation.

The *principal focus* is that point at which parallel rays meet in passing through a convex lens. A concave lens has no real focus, but a virtual focus in the negative direction.

The *principal focal distance* is the distance between the optical center of the convex lens and the principal focus (f). (Fig. 249.)

FIG. 249.

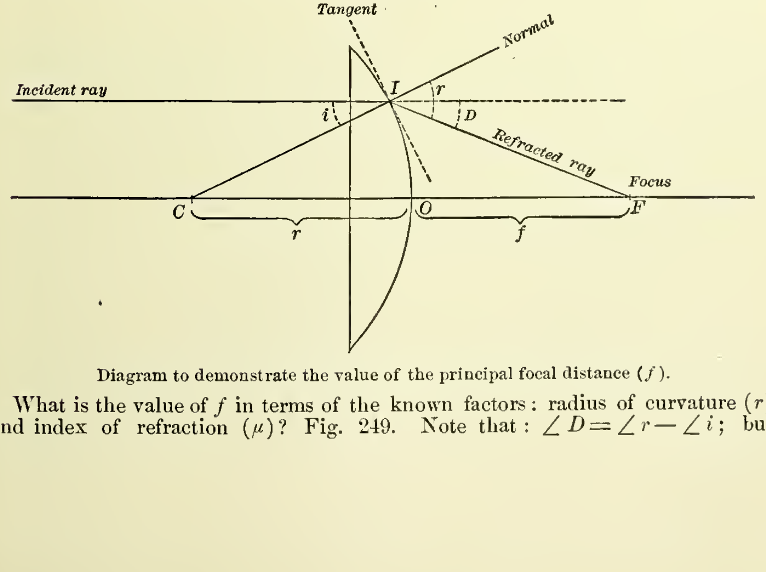
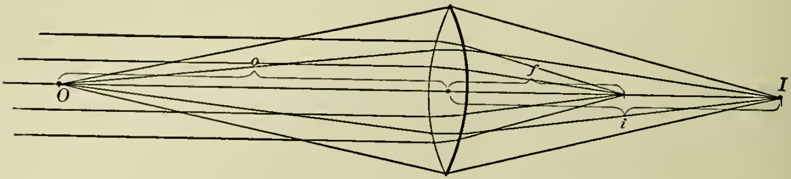


Diagram to demonstrate the value of the principal focal distance (f).

What is the value of f in terms of the known factors: radius of curvature (r) and index of refraction (μ)? Fig. 249. Note that: $\angle D = \angle r - \angle i$; but

PROP. IX. Rays of light emitted from a luminous point in the optical axis will, on passing through a concave lens, be diverged from the optical axis or will become more divergent or less convergent.

FIG. 250.



The relation of the conjugate foci to the principal focal distance.

PROP. X. The sum of the reciprocals of the conjugate focal distances is equal to the principal focal distance,[1] or $\frac{1}{o}+\frac{1}{i}=\frac{1}{f}$, or $f=\frac{oi}{o+i}$ when $o =$ distance of object, $i =$ distance of image, and $f =$ principal focal distance.

$\angle i : \angle r :: 1 : \mu$; let $\angle i = 1$, *i. e.*, let the angle of incidence be taken as a measure: then $\angle r = \mu$; but $\angle D = \angle r - \angle i \therefore \angle D = \mu - 1$. Suppose the point of incidence I to be indefinitely near to O, then $\triangle$s IOF and IOC are right angled at O. $\angle IFO = \angle D$; $\angle ICO = \angle i$. Measure the angles i and D by their common tangent IO which we will call t, then $\angle i : \angle D :: \frac{t}{r} : \frac{t}{f}$; therefore $\angle i : \angle D :: f : r$; but $\angle D = \mu - 1$ and $\angle i = 1$; therefore, $1 : \mu - 1 :: f : r$ or $f = \frac{r}{\mu - 1}$, which was to be determined.

For a biconvex lens, $f = \frac{r}{2(\mu - 1)}$.

[1] *Conjugate Foci.* If the source of light be near enough to the lens so that the rays are not parallel, but divergent, the lens will not bring them to a focus so soon as in the first case, *e. g.*, rays from the point O would be focused at the point I. The distance f is by definition invariable. The distance o and i may vary at will. What is the relation between these distances? (See proposition X.)

To Solve: (1) When $o = 2f$; what is the value of i?
(2) When $o < 2f$; how does i compare with $2f$?
(3) When $o > 2f$; how does i compare with $2f$?
(4) When $o = \infty$; what is the value of i?
(5) When $o = f$; what is the value of i?
(6) Does o vary as $\frac{1}{i}$; does i vary as $\frac{1}{o}$?
(7) Given $o = 20$ cm.; $1 = 20$ cm.; to find f.
(8) Given $o = 100$ cm.; $f = 10$ cm.; to find i.
(9) Given $i = 5$ cm.; $f = 5$ m.; to find o.

Before proceeding with the theoretical application of the laws of refraction to the human eye the student will do well to review again such problems as the following:

A Simple Dioptric System.

The simplest dioptric system is one in which the ray passes from one medium into a second medium of different refractive index, the surface of separation of the two media being a spherical surface. In the accompanying figure (Fig. 251) the spherical surface, s', s, p, s'', separates the medium *M*, whose refractive index is 1 from the medium *M'*, whose refractive index is 1.5.

Fig. 251.

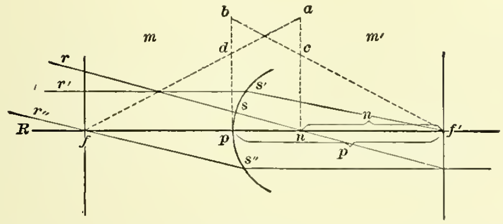


Diagram to show the cardinal points of a single dioptric system.

Note the following *cardinal points* of a simple *dioptric system* :

The center of curvature of the spherical surface (n) in the nodal point.

That radius which is the center of symmetry of the dioptric system (*i. e.*, n, p) is called the *principal axis* of the system. In this axis lie the *first* and *second principal foci*, f and f' respectively. The point where the optical axis cuts the spherical surface (p) is called the *principal point.* The plane tangent to the spherical surface at this point is the *principal plane.* Planes perpendicular to the optical axis at f' and f are called the *first* and *second principal focal planes* respectively.

Given the radius of curvature and the index of refraction to locate upon the principal axis the principal foci.

Problems:—(1) Given a biconvex lens, focal distance $= f$ to construct the image of a point located at $o = 2f$.

(2) Given a biconvex lens, focal distance $= f$; to construct the image of a line whose middle point lies in the optical axis of the lens and at a distance of $4f$ from the optical center of the lens.

(3) Given a biconvex lens whose radius of curvature for both surfaces is equal to its focal distance to determine the index of refraction of the lens substance.

(4) Given a biconvex lens whose radius of curvature is 5 cm., for both surfaces and whose index of refraction is 1.5; to construct the image of a line 2 cm. in length ⊥ to the optical axis and one of whose extremities lies in the optical axis at a distance of 10 cm. from the optical center.

What are the dimensions of the image?

(5) Suppose the object in the above problem be removed to a distance of 20 cm., what is the length of the image? What are the limits of size of image for varying distances of the object.

(6) If the distance of the image remains the same and if its length remains the same how long must the object be in terms of length of image (l), when the object is located at a distance $o = 2f$ from the optical center of the lens. At distance $o = 4f$; $o = 10f$; $o = 100f$; $o = 1000f$?

Neumann has given the following construction:

(I) Erect at n and p perpendiculars to the principal axis. (II) Lay off, upon each, the two indices of refraction of the two media measured from the origin of each perpendicular, in the same linear units used in measuring the radius. In the figure let nc and pd represent the index of refraction of the medium M, and na and pb the index of refraction of medium M'. The continuation of line ad cuts the principal axis in the point f the first principal focus, while the line bc cuts it in the point f', the second principal focus. The geometrical figure shows the following important properties of the dioptric system:

(I) The distance from the first principal focus to the principal point equals the distance from the second principal focus to the nodal point.

(1) Mathematically expressed: $pf = nf'$.

(II) The ratio of the second focal distance (pf') to the first (pf) is equal to the ratio of the index of refraction of the second medium (M') to that of the first (M).[1]

(2) Mathematically expressed: $pf : pf' = \mu : \mu'$.

But if $pf = nf'$, substitute the value in the second equation;

(3)$\ldots\ldots\ldots\ldots\ldots\ldots nf' : pf' = \mu : \mu'$;

assume the medium M to have an index of refraction $\mu = 1$.

(4)$\ldots\ldots\ldots\ldots\ldots\ldots nf' : pf' = 1 : \mu'$.

(5)$\ldots\ldots\ldots\ldots\ldots\ldots pf' = nf' \times \mu'$;

or, more concisely,

(5′)$\ldots\ldots\ldots\ldots\ldots\ldots p = \mu' n$.

(See p and n in Fig. 251.)

This derived property of construction merits a separate formulation.

(III) The distance from the second principal focus to the principal point equals the product of the distance from that focus to nodal point multiplied by the index of refraction of the second medium ($p = \mu' n$); or using values f and f' and r for the first and second principal foci and the radius, the law may be thus formulated: the first principal focal distance plus the radius of curvature equal the product of the second principal focal distance multiplied by the index of refraction of the second medium ($f + r = f'\mu'$).

Note in addition the following facts regarding the effect of such a dioptric system upon light.

---

[1] Refraction and Accommodation of the Eye.—Landolt, p. 85.

1st. The ray rs meeting the spherical surface perpendicularly, will not be refracted at s, but will pass on through the nodal point.

2d. The ray $r's'$, parallel to the principal axis in the first medium is refracted at the spherical surface and cuts the principal axis at f',—it passes through the second principal focus.

3d. The ray $r''s''$, cutting the principal axis at f in the first medium (M), is refracted at s'' and traverses the second medium parallel to the principal axis.[1]

2. COMPARATIVE PHYSIOLOGY OF VISION.

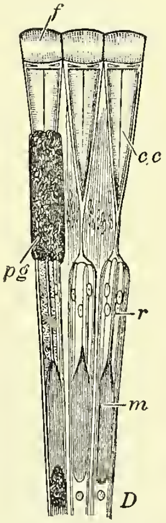
The most primitive manifestation of sensitiveness to light is that manifested by most unicellular organisms. Most protophyta gather upon the best illuminated side of an aquarium. Most multicellular algæ show sensitiveness to light either by movements of the plant as a whole or by movements of the chlorophyll grains within the plant cell. One can recall various examples of light stimulation—heliotropism—in higher plants. But plants have no specialized organs responsive to light; simply primordial protoplasm and the green pigment chlorophyll.

Many *protozoa* show a sensitiveness to light. Pelamyxa and Pleuronema, amœba-like animals, both contract all pseudopodia when light falls upon them. If one side of an aquarium is in deep shade these protozoa present in the aquarium will always be found there.

Many *cœlenterata* possess eye-spots which must be recognized as the most primitive organ of vision. The eye spots are simply patches of pigment which are more sensitive to light than is protoplasm generally.

Echinoderms possess these primitive eyes in a very simple form. The eye spots at the end of a starfish's arms consist of a group of little invaginated pits, the cells of which are developed from a red pigment, and are in communication with the nerve-ring through special sensory nerve-fibers.

FIG. 252.



Part of the compound eye of *Phryganea*, an anthropod. The retinal cells are seen to be united into a retinula, r, which is differentiated into a rhabdom, m, posteriorly; c, c, crystalline cone; f, facet of compound eye; pg, pigment. (From BELL after GRENOCHER.)

Turbellarians (*vermes*) have eyes in which the pigment-containing cells are differentiated from the sensitive cells. Some of these

---

[1] Problems: I. Construct the image of a line whose central point is in the principal axis at a distance (d) from the nodal point.

II. Given the length of the object (λ) at the distance (d) to determine the length of the image (x) in terms of λ, d, and f (the focal distance).

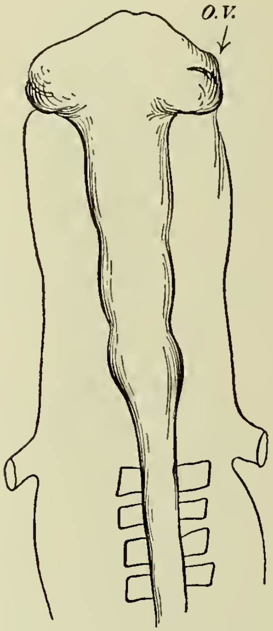
III. Given λ, d, r, f and μ (the index of refraction) to determine the length of the image in terms of λ, d, μ and r.

low worms have several hundred eyes, but the higher worms are represented by the polychætæ, which have a pair in each segment, each eye having a lens, a gelatinous vitreous humor, a layer of rods and a layer of pigment. The common earthworm is blind.

The *molluscs* which are not blind have more primitive eyes than the higher worms. The cephalopod mollusc, however, has a highly developed eye, comprising a cornea, a lens, a ciliary body, a retina with internal and external layers, a pigment layer (choroid), an optic nerve. The eye is subspherical in shape and is protected by spherical fibrous layers homologous with the sclera of a vertebrate's eyes.

The *arthropoda* show a remarkably perfect development in another direction; in the compound eye. The highest crustacea and insecta possess a pair of these eyes, each having many hundred facets each with its minute lens (corneal facet), its pigment sheath and its retinule homologous to retina of a simple eye. (Fig. 252.)

FIG. 253.



Chick. 48 hrs. (KÖLLIKER.)

The *vertebrata* all have eyes not very unlike those of man which may be taken as a type of vertebrate eye.

3. EMBRYOLOGY OF THE HUMAN EYE. (Hertwig's Summary.)

1. The lateral walls of the primary fore-brain vesicle are evaginated to form optic vesicles. (Figs. 253 and 254.)

2. The optic vesicles, remain united by means of a stalk the future optic nerve, with that part of the primary fore-brain vesicle which becomes the Thalamencephalon.

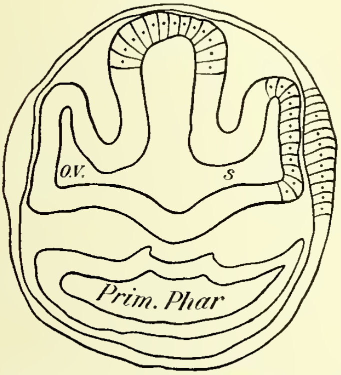
3. The optic vesicle is converted into the optic cup through the invagination of its lateral and lower walls by the fundaments of the lens and the vitreous body.

4. At the place where the lateral wall of the primary optic vesicle encounters the outer germ-layer, the latter becomes thickened, then depressed into a pit and finally constricted off as a lens. (Figs. 255, 256 and 257.)

5. The cells of the posterior wall of the lens vesicle grow out into the lens-fibers, those of the anterior wall become the lens epithelium. (Figs. 257, 260 and 261.)

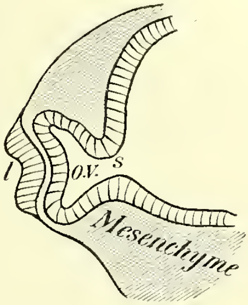
6. The fundament of the lens is enveloped at the time of its principal growth by a vascular capsule (tunica vasculosa lentis) which afterwards entirely disappears except as given in 7.

FIG. 254.



Cross-section head of fish embryo. (BALFOUR.)

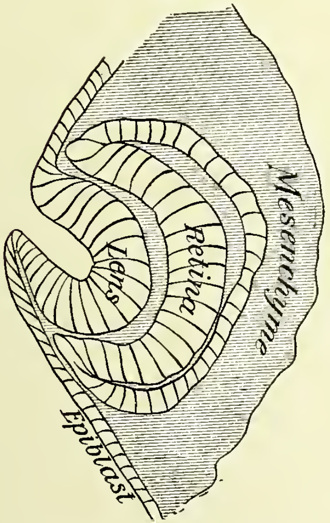
FIG. 255.



From 48-hour chick. (MARSHALL.)

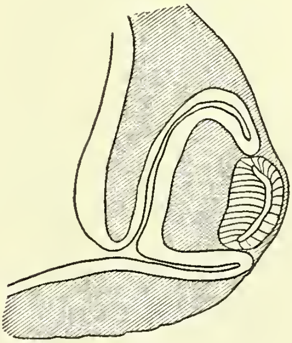
7. Its anterior part becomes the transparent anterior part of the lens capsule. (Fig. 260.)

FIG. 256.



Horizontal-section 54-hour chick. (KÖLLIKER.)

FIG. 257.



Cross-section 64-hour chick. (MARSHALL.)

8. The development of the vitreous body is associated with the formation of the choroid fissure. (Figs. 258 and 259.)

9. The optic capsule has double walls (inner and outer epithelial) which are continuous with each other at the opening of the cup around the lens and along the choroid fissure. (Figs. 256, 257 and 258.)

Fig. 258.

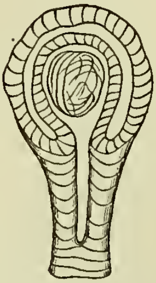
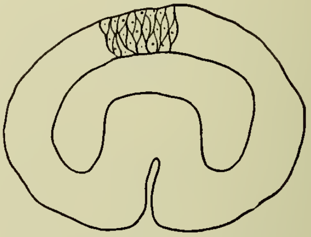


Diagram showing choroid fissure.

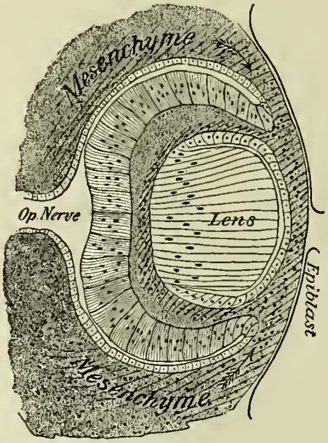
Fig. 259.



Cross-section distal part of optic nerve 13-day rabbit. (Minot.)

10. Mesenchymic cells migrate in between the lens and somewhat closely applied epidermis to form the cornea and Descemet's membrane, the latter being separated from tunica vasculosa lentis by a fissure—anterior chamber (Figs. 260 and 261).

Fig. 260.



Horizontal section 64-day rabbit. (Note invasion of mesenchyme.) (Kölliker.)

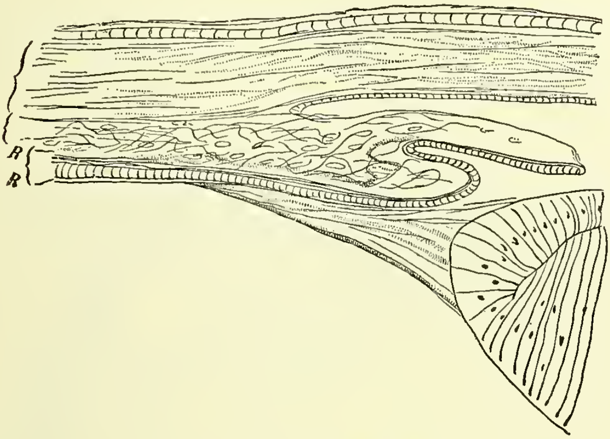
11. The optic cup is differentiated into a posterior part within which its inner layer becomes thickened and constitutes the retina and an anterior part which begins at the ora serrata, becomes much more reduced in thickness and extends over the front surface of the lens, growing into the anterior chamber of the eye until the originally wide opening of the cup is reduced relatively to the size of the pupil.

12. The anterior attenuated portion of the cup is, in turn, divided into two zones of which the posterior zone becomes folded at the equator of the lens to form the ciliary processes, whereas in front it remains smooth, so that the whole cup three parts may be distinguished: Retina propria, Pars ciliaris retinæ, Pars iridica retinæ (Fig. 261).

13. Corresponding to the three portions of the epithelial optic cup, the adjoining mesenchymal envelope (choroid) takes on some-

what different conditions as : (*a*) Choroid proper ; (*b*) Connective tissue stroma of ciliary body and ciliary muscles ; (*c*) Connective tissue stroma of iris and muscles of iris.

Fig. 261.



From section of eye of 13-day chick.

14. The skin surrounding the cornea becomes infolded to form the upper and lower eyelids and the nictitating membrane (rudimentary in man as the plica semilunaris).

15. The epithelial layers of the edges of the two eyelids grow together in the last three months of development but become separated again before birth.

The Development of the Optic Nerve.

16. That part of the central nervous system between the retinal cup and the thalamencephalon is the fundament of the optic nerve. Lieberkühn believed that the nerve-fibers are developed *in loco* from the cells surrounding the hollow stalk. Such fibers would be homologous to intra-central commissural fibers. He observed outgrowths from these cells but he did not trace their course or history.

17. His, Kölliker, W. Müller and others presented the theory that the cells which Lieberkühn described simply formed supporting tissue and that the fibers made their way in from without.

18. His, Kölliker and others believed that the fibers originated in the thalamencephalon and grew outward toward the retina through optic nerve fundament.

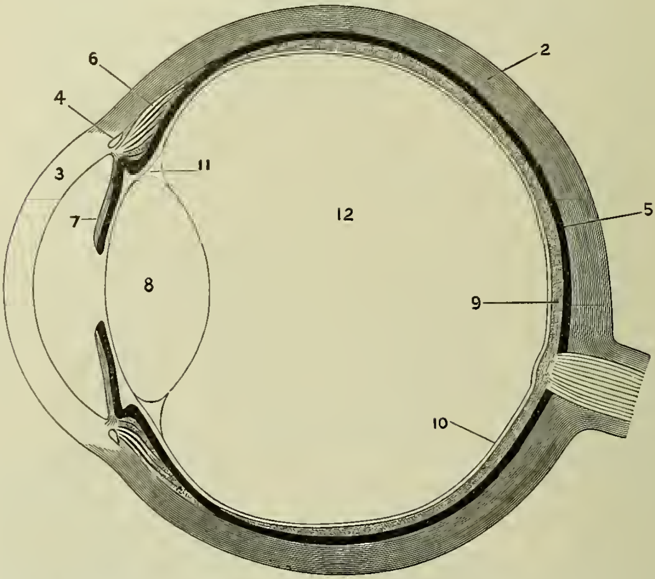
19. W. Müller from observations on petromyzon contended that the fibers grow inward from sense cells in the retina. Later he has been joined by His, Kiebel, Froriep, Kölliker and Edinger.

4. SUMMARY OF THE ANATOMY AND HISTOLOGY OF THE EYE.

The following features of the anatomy of the eye are of special importance in the discussion of *the function of the organ.*

(*a*) The eye is nearly spherical in form and possesses three coats : (I) A very dense strong outer coat,—the sclera, modified anteriorly into a transparent cornea. (Fig. 262, 2, 3.) (II) A very vascular middle layer—the choroid, pigmented to brownish-black color internally. Anteriorly this coat has an aperture—the pupil —and is modified in the region surrounding the pupil into an opaque pigmented contracting and expanding diaphragm. The contraction of the pupil is accomplished by circular muscles while its expansion is brought about by radial muscles. (III) The retinal cup with its outer layer of pigment cells and its inner cerebro-neuro-epithelial layer. The retina is modified anteriorly, possessing a ciliary and an irideal portion which line the ciliary body and iris respectively.

Fig. 262.



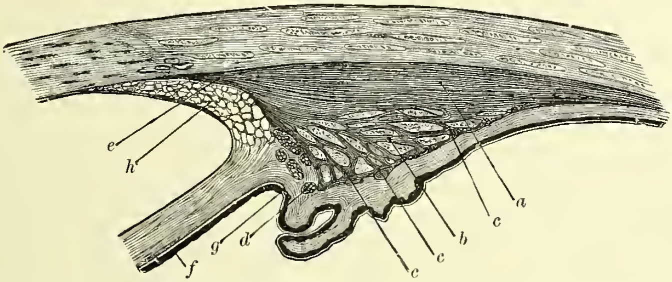
Horizontal section of the right eyeball. 1, optic nerve ; 2, sclerotic coat ; 3, cornea ; 4, canal of Schlemm; 5, choroid coat ; 6, ciliary muscle ; 7, iris ; 8, crystalline lens ; 9, retina ; 10, hyaloid membrane ; 11, canal of Petit ; 12, vitreous body ; 13, aqueous humor. (DALTON.)

(*b*) The eyeball is occupied by the principal *refractive media* of the eye ; (I) The *lens* just behind the iris ; (II) the *aqueous humor* between the lens and the cornea ; (III) the *vitreous humor* back of the lens.

(*c*) The lens is held in position by the *suspensory* ligament whose radiating fibers pass out and come into intimate contact with the pars ciliaris retinæ.

(*d*) The ciliary body (Fig. 263) consist essentially of two sets of muscle fibers : (I) The meridional fibers which extend from the annular tendon (Fig. 263, *e*) backwards gradually merging into the stroma of the choroid as indicated in the figures ; (II) the annular fibers which form a ring around the inner margin of the ciliary body.

FIG. 263.



Section of the ciliary region of the eye in man. *a*, meridional muscular fasciculi of the musculus ciliaris ; *b*, deeper-seated radiating fasciculi ; *c*, *c*, *c*, annular plexus ; *d*, annular muscle of Müller ; *f*, muscular lamina on the posterior surface of the iris ; *g*, muscular plexus at the ciliary border of the iris ; *e*, annular tendon of the musculus ciliaris ; *h*, ligamentum pectinatum. (After FOSTER.)

(*e*) The retina presents an outer layer of black, pigment cells and an inner layer which represents the end-organ of vision (Fig. 264). The inner layer is subdivided into a neuro-epithelial and a cerebral layer. (I) The *neuro-epithelial layer* comprises, besides a supporting epithelium (not shown in the figure) an epithelium sensitive to light. These specialized cells remind one strongly of the fila olfactoria. The rods especially present the elements of a typical neuron : the afferent member (*a*), the body (*b*) and the efferent member (*e*). The *cones* are not very different (see Fig. 264). The efferent member of these epithelial neurons arborize in the *outer reticular layer* with the neurons of the cerebral layer. Like the mitral cells of the olfactory lobe (*q. v.*) these neurons of the second order arborize with several of the epithelial neurons. (II) The *cerebral layer* consists of two series of neurons whose cell bodies form the inner nuclear layer and the ganglion cell layer. These two series of neurons differ slightly as to the disposition of their parts. Those which connect with the cones arborize with the ganglion cells in the inner reticular layer ; those which connect with the rods arborize around the bodies of the ganglion cells in the ganglionic layer. The neuraxons of the ganglion cells pass along the inner surface of the retina, *i. e.*, next to the vitreous humor, to join with the fibers making the optic nerve.

(*f*) The eyeball rests in a bony socket on a bed of fat. It is provided with lids, lashes and brows and a lachrymal apparatus by way of protection; and with four straight and two oblique muscles to direct it. The straight muscles are superior, external, inferior and internal recti. The oblique muscles are the superior and inferior oblique.

FIG. 264.

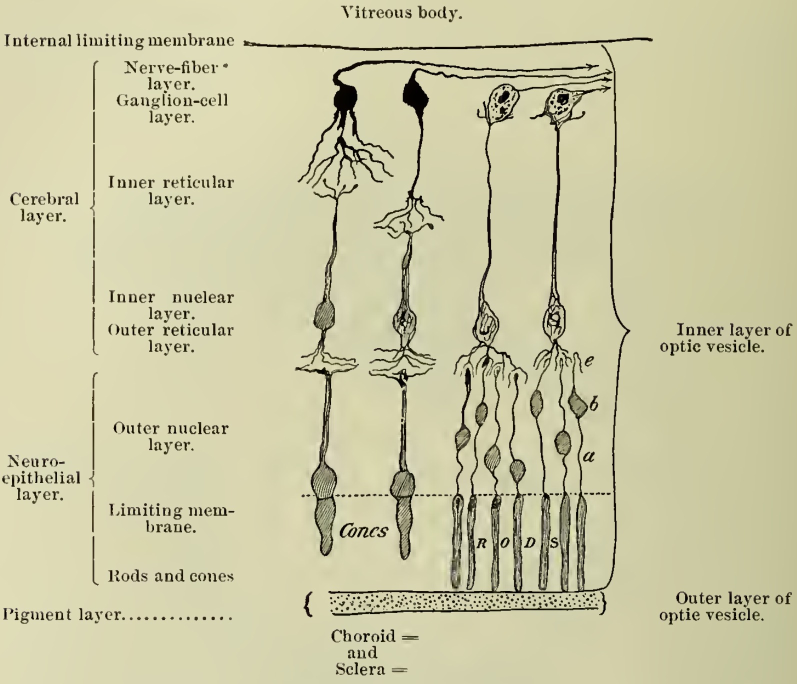


Diagram showing the essential structures of the retina. Note that the upper part of the figure is that which is next to the vitreous body, or the inner surface of the retina, while the lower part is the other surface of the retina. (CAJAL'S figure, somewhat modified.)

THE PHYSIOLOGY OF VISION.

If the student has mastered the general principles of refraction, and has familiarized himself with the structure of the eye he is ready to consider the function of the organ.

Vision comprises two distinct phases of activity: (I) *Optical* in which phase the eye as an optical instrument focuses upon the retina images of objects; (II) *Sensory* in which the sensorium is made conscious of the form and color of the image through the neuro-epithelial cells—rods and cones—and the two orders of sensory neurons.

A. VISUAL OPTICS: THE EYE AS AN OPTICAL INSTRUMENT.

Possessing a lens, with an adjustable focal distance, a diaphragm with an adjustable aperture, a pigment lining for absorption of dispersed light, and a screen for the reception of the image, the eye must at once be recognized as a typical optical instrument. Used as it is for viewing distant objects whose image is infinitesimal compared with the object, the eye resembles a telescope. But the adjustable diaphragm in front of the lens, and the screen for the reception of the image are points which make it more strongly resemble the photographic camera.

All of the optical instruments consist of two distinct mechanisms: (I) *a refractive apparatus* for focusing the rays of light, (II) *a directive apparatus* for directing the axis of the instrument at the object whose image is to be viewed.

1. VISUAL REFRACTION: THE REFRACTIVE APPARATUS OF THE EYE.

Before entering upon the consideration of this topic it might be interesting to note that the mechanical and thermal stimuli of one's environment are quite unmodified preparatory to their stimulation of the sensory end-organs, and the pressures and tensions and temperature act directly upon the sense-organs transmitted practically unmodified through the superficial layers of the cuticle. The chemical agents, however, which serve to stimulate the sensory nerves of smell and taste must enter into solution before the end-organs are stimulated. Furthermore the vibrations of ponderable matter must be condensed and intensified by the transmitting apparatus of the ear before they can sufficiently stimulate the end-organs of hearing.

Finally the vibrations of the imponderable, luminiferous ether can only be recognized as light by the primitive eye spots of the cœlenterates and echinoderms. Nature has, through the lapse of the ages, evolved a visual sense-organ which is able to recognize not only the difference between light and darkness, but also to perceive the form and color of distant objects. In order to accomplish this, rays of light are focused into a clearly defined image through the refractive apparatus of the eye.

a. Application of the Laws of Refraction to the Mammalian Eye.

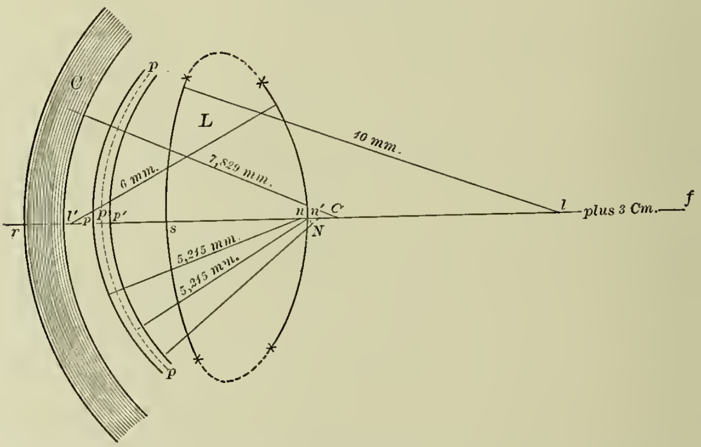
The dissection of an eye reveals several refractive media (cornea, aqueous humor, lens, and vitreous humor) and several curved surfaces bounding these media. In determining the focal distance of a lens one must know the radius of curvature and the refractive index. In determining the focal distance of a system of refractive media and surfaces one must know (1) the radius of curvature of each surface, (2) the refractive index of each medium, and (3) the location of their cardinal points upon the principal axis of the system.

The mammalian eye receives its light through media and surfaces, as indicated in the following:

Media.	Index of Refraction.	Surface.	Radius.
Air.	1.000	……………………	…………………
Tear Film.	1.3365	Over Ant. Surf. Cornea.	7.829+mm.
Cornea.	1.3367	Ant. Corneal Surface.	7.829+mm.
Aq. Humor.	1.3365	Post. Corneal Surface.	7.829—mm.
Lens.	1.4371	Ant. Surface.	10.0 mm.
Vit. Humor.	1.3365	Post. Surface.	6.0 mm.

This array of media and surfaces would seem to make a problem too intricate to solve with the means at our disposal. Notice, first that the tear film and the ant. and post. corneal surfaces have the same radius of curvature; *i. e.*, though curved surfaces they are parallel and form a case under the following theorem: "If a ray pass from any medium through a denser medium which is bounded by two parallel planes it emerges from the denser medium in a line parallel to its course before entering that medium." It is customary at this point to take the anterior surface of the cornea as the first refractive surface and $\mu = 1.3365$.

FIG. 265.



Showing the mathematical features of the reduced eye. For detailed explanation of the figure see text (1), (2) and (3). The figure is multiplied by five in its linear dimensions.

Notice that the index of refraction of the aqueous humor and vitreous humor are the same. It is now evident that we have to deal with three media (air, aqueous or vitreous humor, and lens), with three surfaces (ant. corneal surface, ant. and post. lens surface), whose radii are 7.829, 6 and 10 respectively. But even this great step toward simplifying the problem leaves us with a long road before us unless we can find a short cut. "It has been shown mathematically that a complex optical system consisting of several surfaces and media, centered on a common optical axis, may be treated as if it consisted of two surfaces only." (Textbook of Physiology—Foster, 1891—Vol. IV., p. 9.) The location of these surfaces and the cardinal points is given as follows by Landolt:

1. **The Normal Eye.**—The point r (Fig. 265) where the principal axis cuts the cornea is 22.8237 mm. from the second principal focus f' (the retina); c, the center of curvature of the cornea; s, the point where the optical axis cuts the anterior surface of the lens, is 3.6 mm. from r, the point where the optical axis cuts the posterior surface of the lens 7.2 mm. from r; l, the center of curvature of ant. surface of lens; l', the center of curvature of posterior surface of lens.

2. **The Accurate Mathematical Reduction.**—The reduction referred to in the text above is represented by the two refractive surfaces with nodal points n and n', radii of 5.215 mm. each and cutting the optical axis at p and p', located 1.7532 mm. and 2.11 mm. respectively from r.

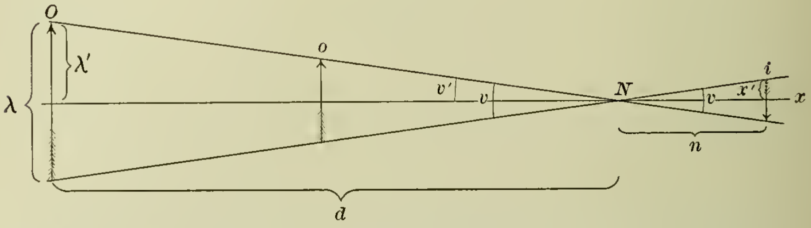
3. **The Final Approximate Reduction.**—Note that p is less than 0.36 mm. from p'. One may assume *one nodal point N*, and *one refracting surface* between the computed ones, cutting the principal axis at P, and introduce an error too slight to be considered. But this brings us back to the "*simplest possible dioptric system*," already described.

Having reduced the eye to a simple dioptric system and having familiarized himself with the optical properties of the simple dioptric system the student may now profitably consider some of the practical applications of the optical properties.

4. **The Visual Angle.**—The visual angle is the angle which the object subtends at the nodal point—the angle v in Fig. 266. This angle is measured by its tangent; for very large angles, *i. e.*, when a large object is viewed at very near range—the tangent should be measured upon the distance d: tangent $v' = \frac{\lambda'}{d} = \frac{x'}{n}$; the angle $v = 2$ angle v'. For medium and for small angles it is sufficiently exact to use the form: tangent $v = \frac{\lambda}{d} = \frac{x}{n}$. It is evident that the object o subtends the same angle as does the object O and its length measured upon its distance gives the same visual angle v; to be concrete: a cent held near enough to the eye

could obscure a great edifice which is some distance away. Helmholtz determined the minimum visual angle to be 50 seconds. The maximum visual angle for direct and distinct vision is not great, say 3°–5°, but varying considerably with different individuals. The maximum visual angle for indirect vision is very great—for a white or luminous body being 50°–60° to the median side of the *line of vision*, 60° above the line of vision, 70° below the line of vision and more than 90° laterally from the line of vision, or over 150° in the horizontal plane and about 130° in the vertical plane. (See perimeter chart, Fig. 273.)

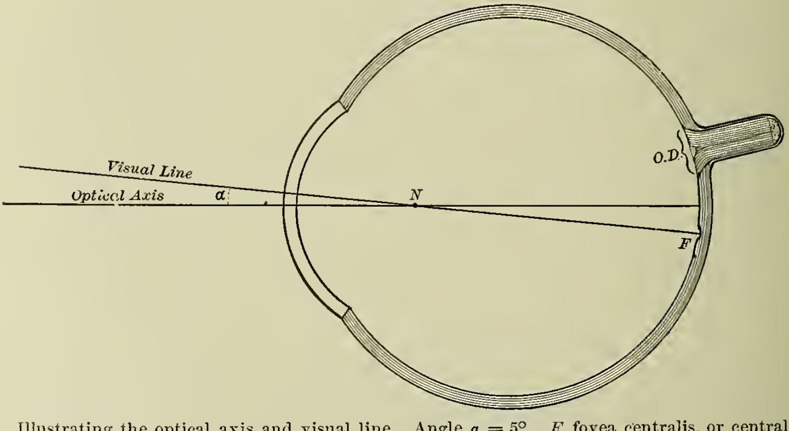
FIG. 266.



Illustrating the *visual angle* (*v*) and the relation of the distance (*d*) to the length of the object (*o*) and image (*i*). *N*, the nodal point; *n*, the focal distance, the image being on the retina.

5. **The Line of Vision.**—Reference has been made to the line of vision. This is the line determined by the nodal point of the eye and the "point of fixation" or the point at which the eye is directed. Within the eye the extended line of vision as just defined meets the retina in the center of the macula lutea, in the *fovea centralis*. This line of vision does not lie in the *mathemat-*

FIG. 267.



Illustrating the optical axis and visual line. Angle $\alpha = 5°$. *F*, fovea centralis, or central pit of the macula lutea; *O.D.*, optic disc, or blind spot, marking the entrance of the optic nerve.

ical axis of the cornea, lens or vitreous humor, but crosses the mathematical-optical axis in the nodal point. It meets the retina between the fovea and optic disc, and passes through the center of the cornea while the line of vision passes the cornea to the median side of the *optical axis.* The angle between the optical axis and the line of vision is one of about 5 degrees. (See Fig. 267.)

6. **The Size of the Retinal Image.**—Given the distance of the object (d) the size of the object (λ) and the distance from the nodal point to the retina (n) it is very simple to compute the size of the retinal image (x) from the equation : $x : n = \lambda : d$ or $x = \frac{n\lambda}{d}$; n is a constant and equals 1.5677 cm. then $x = 1.5677\,\frac{\lambda}{d}$. Express λ and ∂ in centimeters and x will be in centimeters.

To determine the minimum width of the retinal image which is able to excite the sense of vision, *i. e.,* which the subject is able to see ; put a black dot 0.2 mm. in diameter upon a white card and move it away from the eye until it can just be seen. Substituting 0.2 mm for λ in the formula ; $x = \frac{1.567 \times 0.2}{d \text{ (in mm.)}}$, gives the diameter of the smallest visible image.

7. **The Optic Disc or Blind Spot.**—(a) THE LOCATION OF THE BLIND SPOT may be determined as follows (Marriotte's Experiment) : On a white card make a black cross and a circle about three inches apart. Closing the left eye hold the card vertically about ten inches from the right eye so as to bring the cross to the left side of the circle. Look steadily at the cross with the right eye, when both the cross and the circle will be seen. Gradually bring the card toward the eye, keeping the axis of vision fixed upon the cross. At a certain distance the circle will disappear, *i. e.,* when its image falls upon the entrance of the optic nerve. On bringing the card nearer, the circle reappears, the cross of course being visible all the time.

(b) THE OUTLINE OF THE BLIND SPOT may be determined as follows : Make a cross on the center of a sheet of white paper and place it on the table about 30 centimeters from the cornea ; close the left eye and look steadily at the cross with the right eye. Wrap a penholder in white paper, leaving only the tip of the pen point projecting ; dip the latter in ink, or dip the point of a white feather in ink, and keeping the head steady and the axis of vision fixed, place the pen point near the cross and gradually move it to the right until the black becomes invisible. Mark this spot. Carry the blackened point still further outward until it becomes visible again. Mark this outer limit. These two points give the outer and inner limits of the blind spot. Begin again, moving the pencil first in an upward, then in a downward direction, in each case marking where the pencil becomes invisible. If this be done in several diameters an outline of the blind spot is obtained, even little prominences showing the retinal vessels being indicated.

(c) THE SIZE OF THE OPTIC DISC may be readily determined by using the formula given above. Let x equal the long axis of the disc; d the distance from the nodal point to the sheet of white paper upon which the map of the white disc was drawn.[1]

b. Accommodation.

When the normal eye at perfect rest is directed at a distant object the image is formed upon the retina, *i. e.*, the principal focal distance of the resting normal eye is 15.677 mm. As long as the object is sufficiently distant to make the rays of light from any point of the object practically parallel the image is focused upon the retina of the normal eye without any change in the dioptric system of the eye, *i. e.*, with the elements of the dioptric system in the state of rest. The minimum distance to which an object may be brought without requiring a readjustment of the elements of the dioptric system is found to be about 6 m. (20 ft.). In practical ophthalmology this distance is taken as infinity (∞) in all those problems which involve parallelism of the incident rays.

If an object be moved along the optical axis or visual line of a dioptric system the focus will recede and the distance from the nodal point to the image will exceed the focal distance, *i. e.*, the image would be formed behind the retina. The image can be seen only when it is focused upon the retina. The eye possesses the means of adjusting itself to this requirement. The process of adjustment is called *accommodation*. When the object is at infinity—6 meters or more—the distance of the image (i or n) equals the principal focal distance (f). In the process of accommodation the distance of the image is made to equal f. But $f = \frac{r}{\mu - 1}$, therefore the distance of the image depends upon the radius of curvature of the refracting surface and the index of refraction. To make the distance of the image equal the original value of f, *i. e.*, to bring the image back to the retina i must be decreased. The distance of the image $\left(i = \frac{r}{\mu - 1}\right)$ can only be decreased by decreasing the radius of curvature or by increasing the index of refraction; the last alternative is impossible. *The image is focused upon the retina by increasing the radius of curvature of the crystalline lens.* The *process of accommodation is the process of varying the curvature of the crystalline lens.*

1. **The Mechanism of Accommodation.**—Various ways have

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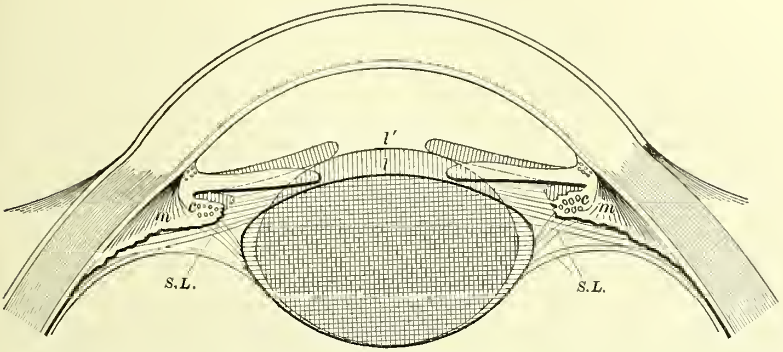
[1] This distance equals the distance of the cornea from the paper plus 7 mm.

been suggested by which the radius of curvature of the lens might be increased ; the theory now generally accepted is that of Helmholtz :[1]

Fig. 268.



Showing the mechanism of accommodation. The horizontally shaded lens and the unshaded iris show the position of the parts when at rest ; the vertically shaded lens and iris show the position during accommodation for a near point. *m*, meridional muscle ; *c*, circular muscle ; *S.L.*, suspensory ligament. (After Landolt.)

(*a*) The Change in the Lens is accomplished through the interaction of two forces : (i) The elasticity of the lens-body ; and (ii) the contraction of the ciliary muscles. The lens when left to itself tends to become more spherical than it is when the eye is at rest ; it tends by its elasticity to take the position *l′* ; but the elasticity of the choroid coat through its relaxed ciliary muscles (*m*) and through its inelastic tendons the "suspensory ligaments" (*S.L.*) exert a still stronger tension in the opposite direction and the lens is flattened and drawn down to the position *l*. All that is necessary to cause the lens to take the position *l′* or any position between *l* and *l′* is for the ciliary muscle to contract, thus relaxing the suspensory ligaments and allowing the lens to become by its own elasticity more nearly spherical. There are two ways of convincing one's self of the increase in convexity of the lens during accommodation.

(*α*) *The direct observation of the change* in the lens may be accomplished by looking from the side at the margin of the iris when the eye of the subject is at rest, *i. e.*, focused upon a distant object. Let the subject suddenly change focus to a very near object. The iris at the margin of the pupil will be seen to advance towards the cornea—pushed out by the lens. (See Fig. 268.)

(*β*) *The indirect observation of the change* may be accomplished by looking diagonally at the subject's eye (Fig. 269, *E*), while a light shines upon the eye from position *L*. The light will be reflected from the anterior surface of the cornea, from the anterior surface of the lens, and from the posterior surface of the lens. When the lens is at rest the images will have to each other

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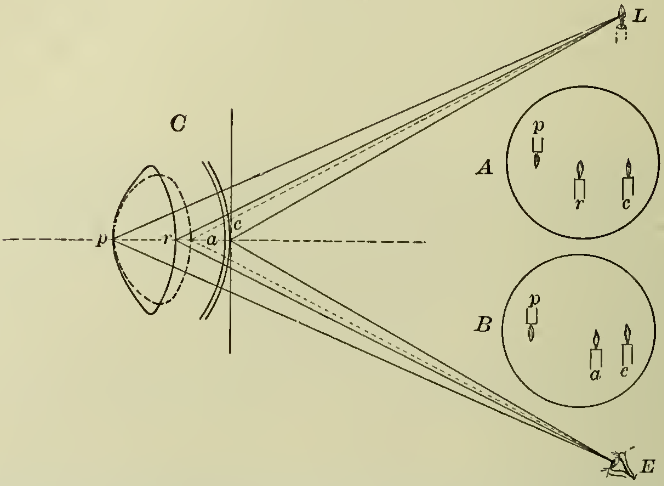
[1] First published in his *Hand-buch der physiologischen Optik*, Heidelberg, 1866. Given in full in the last edition, edited by Arthur König, Berlin, 1896, pages 130–156.

Fig. 269.



Showing the change in the position of the image reflected from the anterior surface of the crystalline lens. *A*, position of images when the eye is at rest ($r + C$) ; *B*, position of images when the lens is more spherical through accommodation ($a — C$); *C*, a geometrical figure showing the reason for the change in position ; *E*, observer's eye ; *L*, candle.

the relation indicated in *A*, Fig. 269. If the subject accommodates, the middle image will move over toward the corneal image, as shown in *B-a*, Fig. 269. The geometrical figure shows how this change is brought about. Utilizing this principle, Helmholtz contrived an instrument which he called the *Phakoscope*.

(*b*) The Pupil Changes its Position both passively and actively. Its passive change, as it is pushed out by the bulging lens, has been referred to above. Its active change may be observed readily if one looks into the eye of a subject from the front, while the subject directs his vision to some distant object. Let the subject then look at a near object and the observer will see the pupil contract. This contraction is accomplished through the action of circular irideal muscles. The reason for the contraction of the pupil is next to seek. One looks at near objects in order to study their detail of structure ; detail of structure can be brought out in an image of a dioptric system only when the spherical aberration, caused by the margins of the lens, is corrected. Work with a microscope soon impresses the fact that for high magnification (near vision) clear definition is possible only when the diaphragm admits rays to the center of the lens exclusively. In the same way in near vision, the eye, by contracting its pupil (its iris diaphragm), brings about a clear definition of the image.

(α) *The most important function of the iris* is that which it performs in conjunction with the lens in the act of accommodation.

(β) *The relation of the pupil to accommodation* is not the sole function of the iris. This changeable diaphragm serves also an important purpose in cutting out an excess of light. If one shade the eyes of a subject and then suddenly allow the light to strike them, the pupil will be observed to contract through the action of the circular muscles of the iris. This is a reflex act in response to the over-stimulation of the retina, the optic nerve acting as a sensory element, while the oculo-motorius is the motor element of the reflex arc.

(γ) In this connection it may be added that *the iris is an important clinical index of certain conditions.* The sympathetic nervous system, from the cilio-spinal center supplies the radiating fibers; so that anything which profoundly affects the sympathetic system will cause a dilatation of the pupil. A strong emotion, especially fear, causes a dilatation of the pupil. In deep chloroform narcosis, or in the last stage of asphyxia, the pupils dilate. The mydriatic drugs (belladonna, atropia, etc.) cause dilatation. Paralysis of the oculo-motorius causes dilatation. The pupil contracts normally during sleep, during accommodation and strong light. When the cervical sympathetic is paralyzed, when a myotic drug—as physostigmin or eserine—is applied locally or opium taken internally the pupil also contracts.

2. **The Range of Accommodation.**—This is the amount of refractive change induced by the eye in adjusting for its point of nearest vision—*punctum proximum*—after it has been at rest, *i. e.*, after it has been adjusted to its point of farthest vision—its *punctum remotum.*

(*a*) To Determine the Punctum Proximum one has only to record in meters the distance from the cornea to the printed page, when the subject can see the lines perfectly clearly; that is without noticing any blurring of the letters. Suppose this distance be 10 cm., then one writes punctum proximum = .01 meter.

(*b*) To Determine the Punctum Remotum let the subject look at an object six meters away. If he can make out the details of the object and can read letters 1 cm. in height and with strokes 2 mm. in width one will credit him with a punctum remotum of *infinity* (∞). If the subject cannot see distant objects bring the object nearer until he can see its details of structure. Let us suppose that it must be brought to a distance of 50 cm. before the subject can make out its details, then one writes punctum remotum = 0.5 m.

(*c*) To Determine the Range of accommodation. Let R = the distance of punctum remotum, then the static refraction, or the refraction when the eye is at rest may be represented by r which is the reciprocal of the distance. (Donders.)

$$\text{(I)} \qquad r = \frac{1}{R}$$

When $R = \infty$, $r = 0$; when $R = .5$ m., $r = 2$.

Let P be the distance of the punctum proximum and p the maximum refraction of the eye.

$$\text{(II)} \qquad p = \frac{1}{P}$$

When $P = 10$ cm., or .1 m., $p = 10$.

Representing the range of accommodation by a or $\frac{1}{A}$, Donders expressed the range in terms of $\frac{1}{P}$ and $\frac{1}{R}$ thus:

$$\text{(III)} \qquad \frac{1}{A} = \frac{1}{P} - \frac{1}{R}$$

$$\text{(IV)} \qquad A = \frac{PR}{R - P}$$

Substituting $R = .5$ m. and $P = .1$ m. we get $A = \frac{.5 \times .1}{.5 - .1} = \frac{.05}{.4} = .125$ m. That is, the accommodation is equal to a lens whose focal distance is .125 m. or $\frac{1}{8}$ m. But that is an 8 dioptre lens.[1] Substituting $R = \infty$ and $P = .1$ m. we get $A = \frac{\infty}{\infty}$ which is indeterminate. In order to avoid this complication and to simplify the process ophthalmologists use the simple equation:

$$\text{(V)} \qquad a = p - r.$$

Substituting $p = 10D$ and $r = 2D$ one gets $a = 8D$ instead of .125 m. Using the formula one avoids the difficulty noted above in the use of Donders' formula; *e. g.*, take $R = \infty$ and $P =$

---

[1] Lenses are now almost universally numbered according to the metric system. A lens with a focal distance of 1 m. is called a 1 dioptre lens or 1 D. A lens of 50 cm. or $\frac{1}{2}$ m. is called a 2 D lens and so on. $\frac{1}{3}$ m. corresponding to $3D$, $\frac{1}{4}$ m. to 4 D, $\frac{1}{5}$ m. to 5 D, $\frac{1}{8}$ m. to 8 D, $\frac{1}{10}$ m. to 10 D, 2 m. to $\frac{1}{2}$ D or .5 D, 4 m. to .25 D, 8 m. to .125 D, etc.

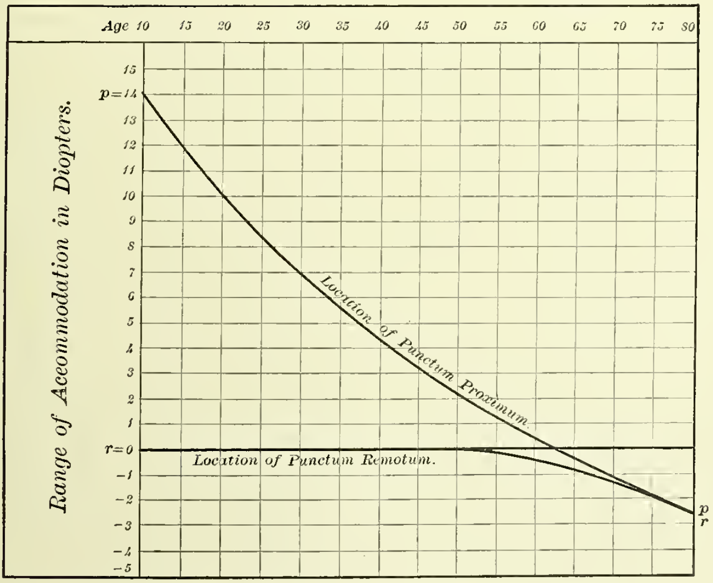
.1 m., then $r = 0D$ and $p = 10D$. $a = p - r = 10D - 0D$ = 10 dioptres of accommodation. Now in certain cases (see Hypermetropia) the punctum remotum is beyond infinity (!).

If the *punctum remotum* is "beyond infinity" that is equivalent to saying that the eye at rest does not focus parallel lines (from infinity) upon the retina, but the lines must be more than parallel, *i. e.*, from *beyond* infinity; or, better, *convergent;* but if they are convergent they would meet behind the cornea. The punctum remotum for hyperopes is then *negative* in direction and is equal to the distance, beyond the cornea, at which the convergent lines would meet if prolonged. It follows that $\frac{1}{R}$ is in the case of hyperopes negative. Our formula (3) would take the form:

$$(3') \ldots\ldots\ldots\ldots \quad \frac{1}{A} = \frac{1}{P} - \left(-\frac{1}{R}\right) = \frac{1}{P} + \frac{1}{R}.$$

Therefore formula (5) becomes (5′) $a = p + r$. Now, in determining r one may use a convex lens of such strength as to give the rays the requisite convergence. The value of the lens in dioptres is, of course, the value of r. In the hyperope a is always greater than p. As the determination of the punctum remotum

FIG. 270.



Curves showing the influence of age upon the location of the punctum proximum and the punctum remotum, and upon the range of accommodation. (After LANDOLT.)

of the hyperotic eye is a matter for the clinician to deal with, we will omit its determination here.

(*d*) THE INFLUENCE OF AGE upon the range of accommodation is well shown in the accompanying chart (Fig. 270). The average 10-year-old boy or girl has a range of ($a = p - r$) 14 dioptres. At 25 years the range has decreased through a recession of the punctum proximum to ($a = p - r = 8 - 0$) 8 *D*. At 45 years it is 3 *D;* at 50 years, 2 *D;* at 60 years, 1 *D*. Note that the punctum remotum begins to recede at 50 to 55 years and at 60 years, $p = +.5$ and $r = -.5$, so that $a = .5 - (-.5) = 1$ *D*.

c. Imperfections of the Refractive Apparatus of the Eye.

It will be remembered that the sole function of the eye as a refractive apparatus is to focus rays from any object, near or far, upon the retina; that when the accommodative (focusing) apparatus is at rest the image of an object 6 m. or more distant is formed upon the retina in the normal eye ($f = i$). The distance of the image depends, then, upon the value of f. But the principal focal distance depends in turn upon the radius of curvature, the index of refraction and the location on the optical axis of the elements of the dioptric system. In the nature of the case the index of refraction cannot change perceptibly. In the principal imperfections of the refractive apparatus of the eye the position of the elements of the dioptric system upon the optical apparatus is faulty. If the screen (retina) is too far back the rays will come to a focus before reaching the retina. The subject will attempt to correct the difficulty by bringing the object near to the eye, thus increasing the conjugate focal distance until the image falls upon the retina. This bringing of the object near to the eye is a sign of a condition of the eye, which has, in consequence, been called *"near-sightedness."* The oculists call this condition *myopia*, and correct it by placing before the eyes concave or divergent lenses which enable the subject to see distant objects.

The retina may be too close to the nodal point; that is, the eyeball may be flattened in the antero-posterior diameter. In that case rays of light from a distant object would not be brought to a focus by the time they reach the retina. The subject will attempt to correct the difficulty by bringing into action the accommodative apparatus of the eye thus bringing the focus nearer to the nodal point until it falls upon the retina and the object is clearly seen. This condition is called far-sightedness or *hypermetropia*. The oculists correct it by placing before the eyes convex or convergent lenses which enable the subject to see distant objects without the help of accommodation.

The radius of curvature of the cornea may be different in different planes. If the radius is shorter in the horizontal than in the vertical plane the rays which lie in that plane will be focused nearer to the nodal point than will those which lie in the vertical plane. It must be evident that the eye would, under such conditions, be quite unable to focus both horizontal and vertical lines at the same time. Bringing the object nearer does not relieve the subject; using the accommodation does not help the condition.[1]

The most effective way of relieving the condition without artificial means is for the subject to bring the eyelids very close together leaving only a narrow horizontal slit. In this way all of the rays are cut out except those in one plane and if these do not fall upon the retina when the eye is at rest the subject may bring the object nearer to the eye or may use the accommodation. This condition of the eye is called, by the oculists, *astigmatism* and it is corrected by placing before the eyes plano-convex cylindrical lenses which increase the curvature of the refracting surface in one plane only. It is only necessary to adjust the axis of the cylinder at such an angle as to increase the curvature in the plane where it is smallest (or decrease it through the use of plano-concave cylinders in the plane where it is greatest) to put the dioptric system into approximately perfect condition.

2. VISUAL MECHANICS.

As the telescope or the camera must be provided with a directive apparatus, by means of which the direction of its optical axis may be changed so the eye is provided with an apparatus for changing the direction of the line of vision. In directing the vision from one point or object to another the axis of the eye is turned upward, or downward, or outward, or inward, or is circumducted, in short, the axis of the eye has an absolutely universal motion within its limits.

a. Monocular Fixation.

The term monocular fixation is used to designate the mechanical adjustment of the eye to bring the image of the object upon the macula lutea, the most sensitive portion of the retina. If one study the movements of one eye (the other being shaded) he will find that it readily follows the movements of an object held in front of it, however, quickly or through whatever angles or directions it may be moved by the observer. The directive apparatus of the eye consists of the six muscles named in the anatomical introduction moving the eye about three different axes of rotation:

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[1] It is held by some ophthalmologists, however, that a modified accommodative act may contract the ciliary muscles in one plane more than in another and thus correct or at least partially correct the condition.

(I) A horizontal axis about which the eye rotates upward and downward; (II) a vertical axis about which the eye rotates from right to left; and (III) a longitudinal axis which coincides practically with the physiological axis or line of vision and about which the eye rotates (slightly) when the oblique muscles are in action. These three axes are rather arbitrarily located. Inasmuch as the eye is a spherical body resting in a hollow spherical socket, and inasmuch as it rotates freely in any direction about the intersection of the three assumed axes it is somewhat simpler to take a central *point of rotation* about which the eye may rotate in any direction whatsoever under the action of one or more of its six muscles.

FIG. 271.

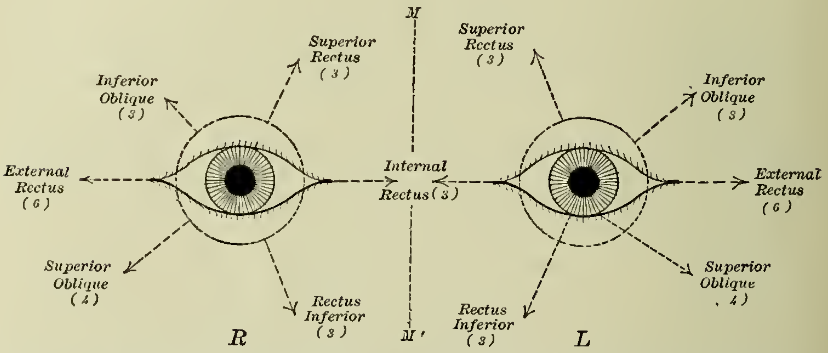


Diagram to illustrate the directions toward which the optical axis is directed or inclined by the contraction of the individual muscles. MM' is the median line; R, the right eye, and L the left one. The numbers in parenthesis (3, 4 and 6), indicate the innervation of the muscle. (After WALLER.)

Waller's excellent diagram (Fig. 271) given in the accompanying figure, will enable the student to interpret the mechanism of the directive power of the eye. Take, for example, the movement of the optical axis of the right eye outward or away from the median line in the horizontal plane. This movement is accomplished by the external rectus innervated by the sixth nerve. Again take the movement of the axis of the eye upward in the vertical plane. It is evident that the superior rectus alone cannot accomplish this; but that that muscle must act in conjunction with the inferior oblique. In a similar manner movement vertically downward requires the combined action of the inferior rectus and the superior oblique.

In general the contraction of a single muscle causes a rotation of the eye in the direction indicated in the diagram for that muscle; while rotation in any other direction than the six which are indicated by the arrows requires the interaction of the two muscles, and frequently the coördinative influence of two nerves. To circumduct the eye, sweeping its axis around a circle requires the action of all of the muscles, acting two or three at a time; an action the exactness of adjustment and the complexity of coördination of which must compel the admiration of any student of mechanics.

b. Binocular Fixation.

This expression is used to designate the coördinated binocular movement which results in directing the physiological axes of *both* eyes upon the same object. If the object fixed by both eyes be a small one its image falls upon the fovea centralis; if it be a large one it will be disposed about that point symmetrically as shown in Fig. 272. The lower part of the object being focused upon the upper segment of the two retinæ, and the right part of the object being focused upon the left part of the two retinæ, that is upon the median segment of the right retina and the external segment of the left retina.

It is evident that we have to deal with a complex mechanical action: (I) With double monocular fixation; and (II) with convergence of the visual axes of the eyes. If one refers to Waller's diagram he can readily tabulate the muscles involved in directing the two eyes in any particular direction. If in Fig. 272 the object O move toward the right eye along the visual axis ONF the fixation of the right eye will not need to be readjusted. If however the visual axis of the left eye $ON'F'$ follow the movement of the object it will have to deflect to the right, thus making a greater angle ($\angle F'Om$) with the median line (mm')

Fig. 272.

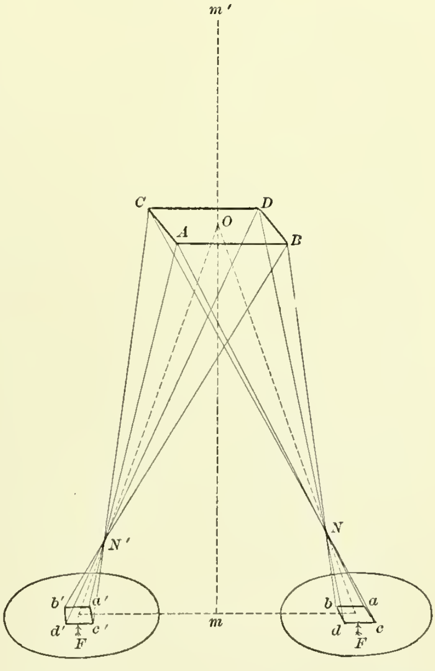


Diagram showing the symmetrical correspondence of the retinal field. N, nodal point; F, fovea centralis. The observer is supposed to be looking down upon the optical apparatus from above. Note that the line CD, which is on the lower side of the object, is the upper side of the image. And that the line BD, which is the right side of the object, is the left side of the image, which brings it at the inner segment of the right retina and the outer segment of the left retina.

than existed before. This increase of the *angle of convergence* is brought about by the internal rectus. If through weakness or through paralysis this muscle is unable to rotate the eye far enough to bring the points O, N', and F' into a straight line then the retinal image would not fall upon the field (a' b' c' d') and there would be a double visual sensation, "double-vision" or *diplopia*. Failure for any other reason to produce perfect binocular fixation leads to the same derangement of vision. This is the principal—though not especially frequent—imperfection of the directive or mechanical apparatus of the organ of vision and is often corrected by oculists through the use of prismatic lenses which bend the optical axis bringing the image upon the proper field of the retina.

B. VISUAL SENSATION.

THE EYE AS THE SENSE-ORGAN OF VISION.

The retina is the end-organ of vision; its function is to receive the impression of the image focused upon its surface by the optical apparatus and to transmit the impression to the brain. About all that can be said is that the lights, shades and colors of the retinal image start in the neuro-epithelial cells metabolic changes which are influenced more or less by the action of the light upon the pigments in the associated tissues. The neuro-epithelial cells are composed of an afferent element represented by the cones or rods of the external layer of the retina that is the scene of the metabolic changes referred to above. The chemical changes start, along the afferent element (dendrite) toward the cell body, an impulse which is transmitted by the efferent element (neurite) to the first neuron of the cerebral layer of the retina, thence by the second neuron to the sensorium of the brain.

The phases of visual sensation which seem most profitable to briefly discuss are retinal stimulation, retinal irritability, and visual sensations.

1. RETINAL STIMULATION.

a. The Stimuli.

(*a*) **The Kinds of Stimuli** which lead to visual sensation are limited normally to: (I) diffuse light in its various colors and to (II) images of objects. In either case the stimulus is light, but it seems expedient in view of what is to follow to differentiate between the light in general and images of objects. The retina, in common with all highly specialized tissues responds to all stimuli with the same general sensation. If one press upon the side of the eyeball a ring of light will be seen upon the opposite segment of the retina. The retina is stimulated under the finger but it is referred to the opposite side. When a mechanical shock to the head makes one "see stars" these luminaries are real sensations due to the mechanical stimulus. Electricity may also produce the sensation of light.

Light being a mode of undulatory motion it may vary in two ways: (I) In the number of vibrations per unit time, (II) in the amplitude of the vibrations. The first variation is comparable to the variation in the pitch of sound and leads to the color scale, the second variation is comparable to loudness and is recognized in the intensity of the sensation.

(*b*) **The Duration of the Stimulus** may be very short. An electric spark whose duration is less than a millionth of a second is long enough to produce a sensation (Waller). The sensation which a stimulus calls forth is of much longer duration than the stimulus itself. This is made evident when one looks at a rapidly rotating wheel; a spoke occupies a particular position for only an infinitesimal fraction of time, yet it calls forth a sensation. In the position which the spoke takes during the next infinitesimal unit of time another sensation is induced; but the sensation of the previous stimulus persists and the two sensations blend. The result of this blending of the images of the rotating spokes is to produce the effect of a solid wheel. In a similar way if a luminous body be attached to the rim of the rotating wheel the sensation which it produces will not be a point of light, but a more or less elongated line of light. The faster the rotation of the wheel the longer the arc of light until finally the speed of the rotation may be great enough to extend the line of light around the whole circumference of the circle in a solid ring of light. Charpentier says that an interval of 0.027 second must elapse between two flashes of light in order that both can be seen separately.

b. The Irritability of the Retina.

1. **Factors Involved in Retinal Irritability.** — (*a*) THE STRUCTURE OF THE RETINA bears an important relation to its irritability. The two kinds of neuro-epithelial cells—the rods and the cones—are not equally distributed over the retina. There are no rods in the macula lutea; this portion of the retina possesses the cones only. The macula lutea is especially sensitive to the fine lines of images focused upon it; *i. e.*, it is the only portion of the retina from which one may receive a clearly-defined image. That portion of the retina outside of the macula lutea is only faintly sensitive to form, but is very sensitive to light and

responds to very slight modifications in the intensity of the stimulus.

(*b*) The RETINAL PIGMENTS bear some relation to the irritability of the retina. Melanin or fuscin is the brownish-black pigment which makes up the pigment layer of the retina. This pigment seems to form a stock from which other pigments may be replenished. *Rhodopsin*, or "*visual purple*," is found in the rods and is, therefore, absent from the macula lutea. *Chromophanes* are red, green and yellow oil globules found in the cones. The chromophanes are not found in the eyes of mammals.

(*c*) VARYING IRRITABILITY OF DIFFERENT AREAS of the retina is probably due to varying distribution of the rods, cones and pigments. The following facts are important in this connection: (I) The macula lutea is the area of clearest definition of form; it is in fact the only area sensitive to the fine structural details of an image. (II) The macula lutea possesses cones, but no rods, and in its most sensitive area—the fovea centralis—the cones are brought into special prominence by the thinning out of all the other elements. (III) The portion of the retina most sensitive to variations of the intensity of diffused light is that portion outside of the macula. (IV) The portion of the retina outside of the macula is richly studded with *rods*, and each rod possesses its supply of rhodopsin. (V) A solution of rhodopsin bleaches in the light. The retinal image may be actually "fixed" by treating with 4 per cent. solution of potassium alum, the retina which has just been removed immediately after thorough exposure following rest in the darkness. The "fixed" image is called an *optogram*.

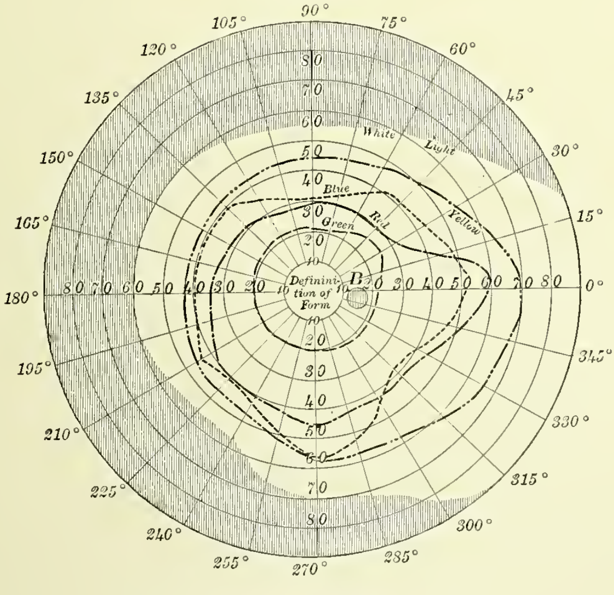
These facts seem to justify the conclusion that *the cones are the structures which receive form-pictures and the pigmented rods are the structures which receive light and color impressions.*

2. **Direct and Indirect Vision.**—These terms designate respectively the central field of clear definition and the surrounding field of indistinct definition. One may get a very good idea of the difference between direct and indirect vision by holding before one eye (the other being shaded) at a distance of 30 cm. a printed page. Direct the line of vision at a small word; the surrounding words will be recognized for a distance of perhaps 2 cm. in any direction, but by studying the sensation very carefully, keeping one particular letter constantly fixed in the line of vision, that one letter is the only letter upon the page that is absolutely clearly defined. The image of that letter lies upon the center of the fovea centralis, the two adjacent letters lie upon the slanting sides of the fovea, their definition is only slightly less distinct than that of the central letter. The form of the next adjacent words can be made out with sufficient clearness to enable the observer to say definitely what the words

arc but he would be quite unable to detect any slight typographical imperfections in the words. The field of direct vision may be taken to be that which is focused upon the macula lutea which is 1.25 mm. in diameter, subtending about 5° of angle at the nodal point.

(*a*) Indirect Monocular Vision.—The field of indirect vision includes all of the visual field outside of that of direct vision. The accompanying figure (Fig. 273) shows the field of indirect vision for white light bounded by the shaded portions of the figure. Note in the center the 5° circle of direct vision within which the form and structural features of objects are clearly defined. Note the blind spot (*B*) at the right of the macula in the figure, and showing that the optic nerve enters the eye to the median side of the fovea located from 12.5° to 17.5° from the center and a little above the horizontal line from the fovea. Note that the boundary of the field for the indirect vision of the white light crosses the upper vertical meridian at 55°, the median meridian at 60°, the lower vertical meridian at 70° and the external meridian beyond 90°. The determination of the line bounding the field of vision is called *perimetry*, the record and the instrument used in getting it, a *perimeter*. The field for

Fig. 273.



Perimeter chart with tracings. (Krapart.)

yellow light is within that for white, the field for blue light is within that for yellow, the field for red light still further withdrawn from the periphery, and the field for green very much smaller than that for red. Perimetry has considerable clinical importance because in certain pathological conditions the perimeters are considerably modified either by being generally contracted or by being dotted with islands of total or partial blindness.

(*b*) INDIRECT BINOCULAR VISION.—To determine just what the field of indirect binocular vision is one has only to find the overlapping areas of indirect monocular vision when both eyes are directed to the same point. The accompanying figure (Fig. 273) is for the right eye. If one trace upon the same chart the field sensitive to white light in the left eye the open external end of the field will extend off to the left and the circular median end to the right reaching the 60° circle. The right and left perimeters will thus overlap in an almost circular area bounded right and left by the 60° circle, above by the 55° circle and below by the 70° circle. The field thus bounded is that for binocular indirect vision for white light.

2. VISUAL SENSATIONS.

a. Fundamental Sensations.

The sensations which light induces in the sensorium may not be so easily differentiated as are those of sound, but they are closely analogous to sound. In sound we differentiate pitch, loudness and quality, dependent respectively upon number of vibrations per unit of time, upon the amplitude of the vibrations, and upon combinations of overtones ; in light we differentiate *color*, *intensity*, and *form* dependent respectively upon number of vibrations per unit time, upon the amplitude of the vibrations and upon combinations of intensities (lights and shadows).

1. **Form.**—The sensation of detail in structure is clearest at the fovea centralis and decreases progressively in every direction from that point in the retina. That this specialization of form-sensation is in some way connected with the fact that, of the rods and cones, cones only are present in the macula and these are brought into special prominence in the fovea, has been suggested above. But the color sensation is also induced by stimulation of the fovea, though Kühne and others show that differentiation of color is less acute at the fovea than in area outside of it.

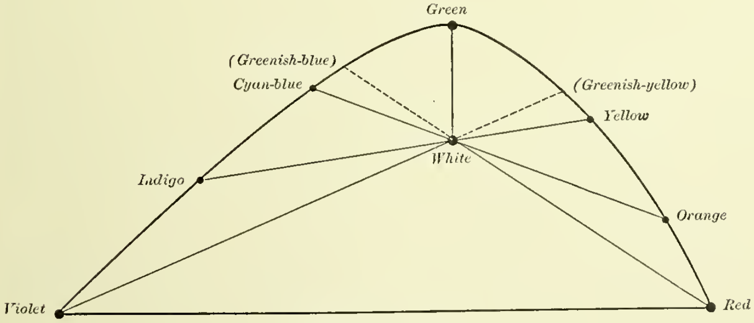
2. **Intensity.**—Intensity depends upon the amplitude of the vibration of the medium which last transmits the light to the eye. As in the case of intensity of sound this may depend upon the

amplitude of vibration of the sonorous or the luminiferous body, or upon the summation of the effects of several vibrating bodies. The sound produced by two sonorous bodies of the same pitch and amplitude will be more intense because of the summation of the undulations; in the same way the light produced by two candles will be more intense than that produced by one.

The sensation induced by lights of varying intensity is not commensurate with the intensity, but obeys Weber's law of sensation: "The smallest change in the magnitude of a stimulus, which one can appreciate through a change in one's sensation always bears the same proportion to the whole magnitude of the stimulus. (As formulated by Foster.) Applied to vision, the proportion is 1 to 100, that is, 0.1 candle-power added to or subtracted from a 10-candle-power light, 1 candle added to or subtracted from a 100-candle-power light, and 10 candles in a 1000-candle-power light can be detected, and so on.

3. **Color.**—Color depends upon the number of vibrations of a luminous body; as pitch depends upon the number of vibrations of a sonorous body. The white light that comes from the sun may be readily decomposed into a number of principal colors and an innumerable number of intermediate mixtures. The principal colors have the following rate of vibration: Red, 392 trillions of vibrations per second; orange, 532 trillions; yellow, 563 trillions; green, 607 trillions; blue, 653 trillions; indigo, 676 trillions; violet, 757 trillions. These vibrations range in wave-lengths from 766 millionths of a millimeter to about half of that length. The colors named above are the principal or the clearly pronounced colors of the spectrum; from three of these all other colors may be produced, these three are the fundamental or *primary colors: red, green, violet.* The accompanying figure (Fig. 274) shows graphically the relation which these colors bear to

FIG. 274.



Geometrical color table.

each other. Not only does a combination of all of the colors produce white, but a combination of certain of the colors in pairs produces white; these pairs are called complementary colors: (I) red and greenish blue; (II) yellow and indigo; (III) orange and cyan blue; (IV) violet and greenish-yellow.

How the different colors can stimulate the retina has been the subject of considerable controversy.

(*a*) THE YOUNG-HELMHOLTZ THEORY, assumes that there are in the retina three different kinds of sensory elements which respond to the three different primary colors,—red, green and violet,—and that "*every color of the spectrum excites all of the elements, some of them feebly, others strongly*" (Landois). The perception of color is then a resultant of the combined sensations brought to the sensorium by the three sets of elements.

(*b*) THE HERING THEORY is based upon the principles of metabolism and upon the color-law of Grassman: "If two simple but non-complementary spectral colors be mixed with each other they give rise to the color-sensation which may be represented by a color lying in the spectrum between both and mixed with a certain quantity of white;" *i. e.*, every color sensation except those of the primary colors may be produced by a color of the spectrum plus white. Hering assumes: (I) That light produces metabolism in the retina; (II) that the metabolic processes are in part anabolic and in part katabolic; (III) that white, red, and yellow sensations are katabolic, *i. e.*, accompanied by disintegration and fatigue; and that black, green, and blue sensations are anabolic, *i. e.*, accompanied by integration and rest; (IV) these metabolic processes are assumed to be paired; *i. e.*, white and black sensations affect the same visual substance in opposite directions; red and green stimulate another visual substance; and yellow and blue stimulate a third. Now according to Grassman's law of color sensation: Any color sensation, except that of a primary color, may be produced by a color of the spectrum plus white. Hering assumes that white visual substance is katabolized not only when one sees white but incidentally in all color sensations except primary ones.

(*c*) THE FRANKLIN THEORY is not antagonistic to either of the foregoing, but rather supplementary. It is based upon the facts of comparative physiology, and assumes that the rudimentary eye distinguishes between light and dark only and possesses neither form nor color senses; so that the fundamental point of departure is a sensation of simple light or dark (Hering's white and black sensation) produced by stimulation of a fundamental "*visual gray*" which causes an accentuation of either the white or the black in it,—(presumably by modifications in the metabolism set up). This theory assumes that the yellow-blue substance was next developed and the red-green last.

The adherents of either the Young-Helmholtz or the Hering theory, especially the latter, may well accept the Franklin theory as supplementary, as it accounts easily for the fact that red-green color-blindness is most common, and yellow-blue blindness rather rare, while inability to see black and white is only found in cases of congenital, total blindness. Furthermore, reference to the perimeter chart shows that white-black covers the largest area of the retina, yellow-blue an area within that which red-green is smallest and quite near the center.

b. Secondary Sensations.

1. **After-images.**—If one fix the gaze upon a brightly illuminated figure or pattern for 15 seconds and then direct it toward a plain surface the image of the pattern gazed at will be seen upon the plain background of the second field of vision. If the after-image has the same colors as the first it is called a *positive after-image.* Positive after-images are usually caused by strong stimuli of short duration rather than by moderate stimuli of long duration. If the after-image is in the complementary color of the original pattern it is called *a negative after-image.* If one gaze intently at a green pattern then turn to a red field the pattern appears deep red upon the red field. It will also appear red upon a neutral field. *Negative after-images are a sign of retinal fatigue.*

2. **Contrast.**—Contrast is the accentuation of a color-sensation through contiguity or succession of another color, especially a complementary color. A piece of note-paper may look white upon a black background, but if it is put upon a really white background it will be seen to be far from white. In a similar manner blue or yellow accentuate each other as do red and green. Various other combinations have this reciprocal effect. If the effect is produced by looking at the two contrasting colors at the same time the sensation is called *simultaneous contrast;* if by looking at the contrasting colors one after another it is called *successive contrast.*

c. Color-Blindness.

Of the male population 4 per cent. or 5 per cent. and of the female population about 1 per cent. are unable to differentiate certain colors. Such persons are called "color-blind."

1. **Complete Color-blindness.**—(Achromatopsy.) Individuals thus afflicted can distinguish lights and shades but have no color sense whatever. According to the Hering theory they lack both the red-green and the yellow-blue visual substance; according to the Franklin theory they represent cases of arrested development of color sense in a condition representing a very primitive condition when only the mental color substance is present.

2. **Yellow-blue Blindness.**—In this condition the blue end of the spectrum is absolutely dark and the yellow may be more or less *illuminated* but void of *color*. This represents also an arrest of development; but this arrest occurs after considerable progress has been made.

3. **Red-green Blindness.**—By far the most common form of color blindness, this is assumed by the Franklin theory to represent the last step in the development of the color sense and, therefore, the first to fail in case of an arrest of development.

4. **Acquired Color-blindness** may result from disease of the retina.

5. **Normal Color-blindness** exists in the periphery of the retina. Passing from without inwards the outermost sensation is that of white (and black); the next that of yellow and blue, followed by red and green. (See Perimetry.)

3. VISUAL PERCEPTIONS AND JUDGMENTS.

One may have a sensation of black lines upon a white surface without perceiving in the lines a letter or word. The retino-cerebral apparatus brings to the sensorium of the untutored savage the same sensations as it does to the sensorium of the scholar. The savage "senses" a written word upon a page, but does not *perceive* it; on the other hand, the scholar may "sense" the twigs upon the forest path without perceiving in their position and condition the track of an animal. Simple sensation involves nothing higher than the sensorium. There is no reason to believe that the sensorium brings to the consciousness of different individuals different sensations. Perception involves cerebration in the interpretation of sensations. Perception involves previous knowledge or memory of the same or related sensations. Effectual perception, like effectual marksmanship, depends upon the man behind the instrument.

Visual perception is the *seeing with understanding*. *Visual judgments* are based upon visual perceptions and represent conclusions reached after comparison of previous perceptions.

a. Acuteness of Vision.

It is frequently necessary to test the acuteness of vision through a comparison of visual perceptions. An individual whose acuteness of vision is in question presents himself to the ophthalmologist for examination. If the subject is schooled in interpreting dim and distorted images he may mislead the observer for a few moments with his acute perception, but the faulty sensation must sooner or later reveal itself. The observer will present to the subject a series of letters in unusual combinations, so that there will be no way in which he can get a clue for his judgment to work upon.

To be more concrete: The acuteness of vision is tested by reading letters of various heights at various distances. The normal eye (emmetropic eye) should see clearly at 6 m.—the oculist's infinity—letters which subtend an angle of 5′; *i. e.*, letters $1\frac{1}{6}$ cm. in height. At 12 meters the normal eye should distinguish and name letters which are $2\frac{1}{3}$ cm. in height. These letters subtend an angle of 5′—the minimum angle of clear vision. If the individual can see at 6 m. only what he should see at 12 m., he is credited with: $\text{Vision} = \frac{6}{12}$; if he can see at 6 m. what he should see at 30 m., he is credited with: $\text{Vision} = \frac{6}{30}$. If by cultivation the visual power has been brought up above the average so that he can see at 6 m. what the average eye must bring to 3 m. to see, he will be credited with: $\text{Vision} = \frac{6}{3}$.

The acuteness of vision varies much with the habits and employment of the individual. Persons employed at fine, close work acquire a microscopic vision; *i. e.*, ability to see and interpret the minutest detail of structure. Persons employed in vocations which require long-distance vision acquire telescopic eyes; *i. e.*, ability to see and interpret structure of distant objects. Sailors and rangemen possess this ability to a marked degree.

b. Visual Estimates.

1. **Estimate of Distance.**—This judgment is based upon a combination of at least two sensations or perceptions: (I) sensation of the accommodation required to focus the image of the object upon the retina; (II) the sensation of the convergence required to direct the two visual lines at the same object in the binocular vision. These sensations are examples of muscular-sense. One estimates these muscular efforts instinctively. Upon these instinctive estimates one bases his judgment of the distance of an object. But other considerations may enter in to assist in the estimate of distance. For example, a movement of the head or body causes a displacement of nearer objects in the background formed by more distinct objects; one learns by experience how much this displacement should be for given distances and bases his judgment accordingly. The known size of an object is an important factor in the estimate of its distance. In this estimate one instinctively measures the image and compares it with the image of the same object at a short distance.

2. **Estimate of Size.**—This judgment is based upon two perceptions: (I) the size of the image; and (II) the distance of the object. Various other considerations may enter in to modify the judgment.

The subject of visual illusions belongs more properly to psychology than to physiology and will, therefore, not be discussed here.

CHAPTER XI.

THE PHYSIOLOGY OF THE NERVOUS SYSTEM.

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    b. *Types of Neurons.*
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    d. *The Neuronal Cell-body.*
    e. *The Dendrites.*
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C. COÖRDINATION AND EQUILIBRIUM: THE PHYSIOLOGY OF THE CEREBELLUM OR METENCEPHALON.

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D. VISION, COÖRDINATION OF EQUILIBRATION-MOVEMENTS: THE PHYSIOLOGY OF THE MID-BRAIN OR MESENCEPHALON.

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THE PHYSIOLOGY OF THE NERVOUS SYSTEM.[1]

A. THE NEURON: STRUCTURAL AND FUNCTIONAL UNIT OF THE NERVOUS SYSTEM.

1. THE STRUCTURE OF THE NEURON.

IN the study of the physiology of the nervous system, a definite comprehension of the neuron is, perhaps, the first requisite. The older manner of regarding the nervous system as functioning according to its larger anatomical divisions and their inter-relationships, gave place to that which recognized the nerve-cell and the nerve-fiber as the basal elements of nerve-function; this idea has in turn given way to the more exact conception of the neuron forming the functional unit of this mechanism, which in the human organism reaches its highest development. Only within the last two decades has investigation enabled us to predicate with certainty, that all nervous phenomena depend upon the functional activity of these units, and only within the last ten years have we learned with definiteness the nearer nature of these units.

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[1] For the embryological introduction to this chapter the student is referred to the chapter on Reproduction and Development of the Embryo, p. 617 et seq.

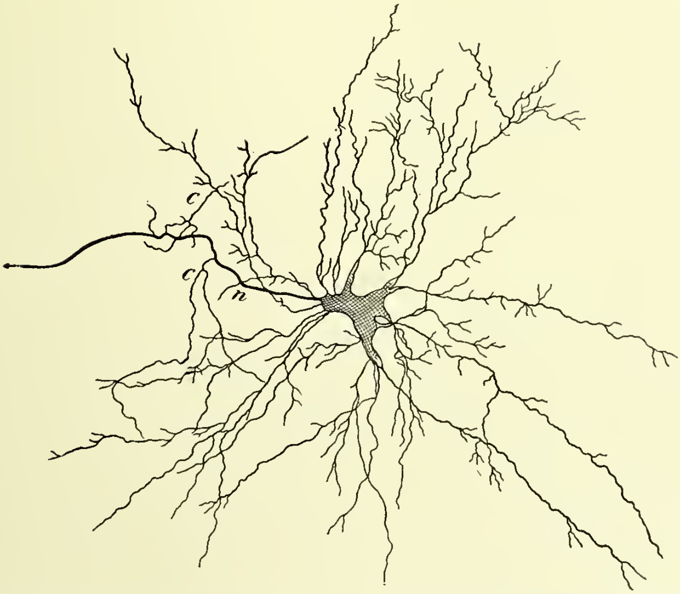
For general introduction the student is referred to the chapter on General Physiology, p. 94 et seq.

Furthermore, it is assumed that a study of the anatomy of the nervous system has been made; and, therefore, to the largest extent possible it will be sought to avoid entering that field here.

(*a*) **General Description.**—The term *Neuron* signifies a nerve-unit, or a nerve-cell with its processes. Waldeyer first used it in 1891.

Recall from embryology the formation in the impregnated ovum of three distinct cell-layers, of which the external one, the epiblast, by a process of dipping in, forms the primitive streak or groove. This groove sinks still deeper into the subjacent mesoblastic layer, its edges finally fusing to form of it a canal, extending the length of the embryo, and, eventually separated from the superficial epiblastic membrane, forms the primitive cerebrospinal axis; in this way we remember the epiblastic origin of the nerve-cell, *the neuron.* Following a little further, one sees how this canal, the central canal, with its epithelial lining develops, at the cephalic end, the complex brain, and how the rest of the tube develops into the intricate structure of the spinal cord, from which cerebrospinal axis there separate off, in time, isolated foci of epiblastic cells, which we later come to recognize as ganglia, situ-

FIG. 275.



Golgi's cell—type I. Cell from the optic tract of the cat laterally from the lateral geniculate body. Radiating from the cell-body are to be seen very many protoplasmic processes which show a broad wedge of origin and branch characteristically; the single axis cylinder process, *n*, has a smooth surface and tolerably even caliber, which is maintained for a considerable distance from the cell. It gives off a few delicate lateral branches or collaterals, *c*. (After KÖLLIKER.) Fig. 59, referred to above, is also an example of Type I.

ated either in close proximity to, or remote from the central axis; and at last, in the fully developed fœtus, a minute examination of the entire nervous system reveals nothing but a complex proliferation of epiblastic cells, the neurons, with their supporting connective tissue and their blood-supplying vessels. Further, in its later, fuller development, we discover but a greater wealth of neurons, to account for the vastly augmented phenomena of nervous activity in adult life.

The cell-body is of different sizes and shapes in different portions of the nervous system. In the ganglia of the posterior spinal roots, unipolar cells are found; in the cortex of the brain there are bipolar cells, and in various parts of the nervous system, multipolar cells, as in the motor centers in the cerebral cortex, and in the anterior horns of the spinal cord. (For figure of a typical neuron, see Fig. 59, p. 95). These cell bodies, of various shapes and sizes, are made up of protoplasm, contained within a limiting membrane. This protoplasm presents a delicate fibrillated structure, the fibrillations seeming to be continuous with the component fibrils of the axon (see below). Besides the fibrils, the cell protoplasm is more or less charged with fine dark granules, the "dark bodies of Nissl." Occupying a fairly central position in the cell-body is one relatively large nucleus, with a distinct nucleolus. The cell-bodies are most numerous in the gray matter of the nervous system, cerebral and cerebellar cortices, basal ganglia of brain, gray matter of pons, medulla oblongata and spinal cord, and in the ganglia throughout the body.

The neuroblasts, or embryonic cells from which are developed the neurons, are isolated oval or pear-shaped cells (His) without processes. Later, at the end of the cell directed away from the epiblastic surface, there arises a process, which becomes the *axis-cylinder* process, *axon*, neurite or neuraxon. Subsequently from the opposite extremity of the cell-body appears one or several processes, the *dendrites*. These, as the name indicates, divide into numerous branches, like the limbs of a tree, and they increase in number and in extent, as their function, in its development, becomes more and more involved. Embryologically then, it will be seen that both the axon and the dendrites grow out of the cell-body.

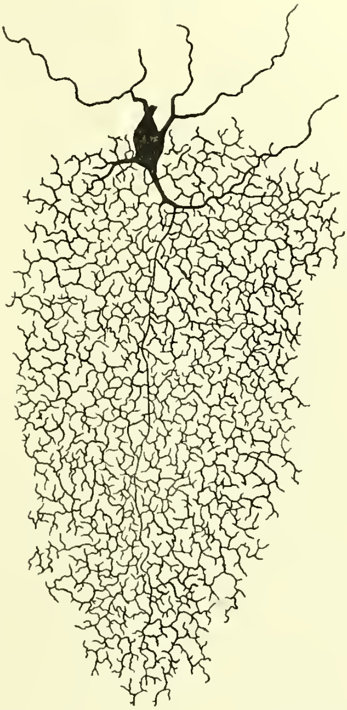
(*b*) **Types of Neurons.**—Morphologically, Golgi was able to distinguish two general types of neurons, which have been generally adopted, and are spoken of as Golgi's "cell-type I" and "type II."

"The cell-type I, as described by Golgi, agrees, in the main, with the general description of a central nerve-cell given by Deiters, being characterized by much-branched protoplasmic processes (usually multiple) and the single axis-cylinder process. That the latter was unbranched, however, as Deiters maintained, Golgi denied, and the discovery of side branches (or collaterals) upon the axis-cylinder processes, first of the pyramidal cells of the cerebral cortex, and later upon those of the Purkinje cells of the cerebellum, represents an advance of a degree of importance utterly beyond Golgi's conception at that time.

"These side branches given off by the axis-cylinder process of cell-type I, were usually delicate and exercised a hardly perceptible influence upon the caliber of the main fiber, which retained its individuality at least for a long distance from the cell. Golgi noted that these side branches existed also upon the motor fibers of the anterior horns (since disproved) and that similar ones were given off by the fibers of the white fasciculi of the spinal cord, whence they ran into the gray matter."

The distal extremity of the axon usually breaks up into an arborization, the single branches of which are in a relation of contiguity with the dendrites of another neuron, or as in the case of a peripheral motor neuron, are flattened out on the muscle fibers, forming the end-plates of the nerve.

Fig. 276.



Golgi's cell—type II. Nerve-cell with short branched axis cylinder from the granular layer of the cerebellum of a cat aged eight days. (After Van Gehuchten.)

Cell-type II differs from type I, characteristically only in the branching of the axon. In type II this process begins to divide very soon after its exit from the cell-body, into a large number of minute branches, forming a dense arborization, whose main branch is distinguishable only a short distance from the cell-body.

Golgi's inference that cell-type I is motor while cell-type II is sensory has since been disproved.

(c) **Interrelations of the Neurons.**—A point of great importance, with reference both to the physiology and the pathology of the nervous system, is the independence of each individual neuron as regards all other neurons, histologically. His and Forel were the first to enunciate this doctrine. It had previously been held that the branching processes of neighboring neurons formed a true net-work, by a species of anastomosis, so to speak. But His, from embryology, and Forel, from pathological anatomy and experimental pathology, were able to state the principle of contiguity as explaining the interrelationships of neurons,—a principle now generally accepted as true, although future more minute microscopical investigation may disclose a joining together of the ultimate branches of correlated neurons. Within the last ten years our knowledge of the structure of neurons has been greatly enriched by the researches of Ramón y Cajal. He has given us: (α) Confirmatory evidence of the independence structurally of each neuron with reference to the rest, the collateral branches from the axons forming anastomoses no more than the dendrites; (β) A fairly correct idea of the great numbers and significance of these axonic collaterals; and (γ) A demonstration of the general similarity of structure of the neurons everywhere, notwithstanding the fact of many minor dissimilarities.

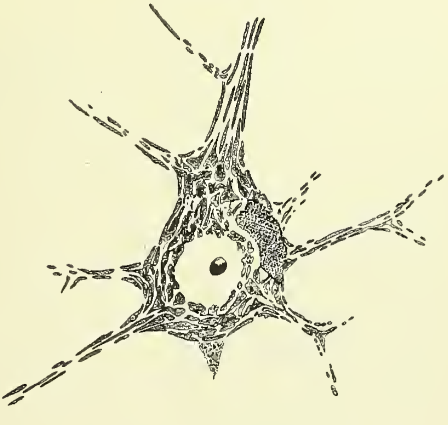
From his study of the axonic collaterals Ramón y Cajal was able to state that they leave the axon by wedge-shaped buddings, almost at right angles to it. Such branches in the spinal cord penetrated deeply into the gray matter and formed free arborizations among cells there located, coming into relation with their dendrites. They were met with fairly constantly in the white tracts of the spinal cord, but are probably not to be found on the axons constituting the ventral roots of the cord. A peculiar disposition of the axons making up the posterior roots was observed. Here the axon arises from a cell in the ganglion located on the root, and passes into the posterior part of the cord itself. Upon entering the cord it divides distinctly into two branches, one ascending and one descending, both becoming longitudinal in the posterior columns of the cord. From them both collaterals pass horizontally to communicate with cells at various levels in the gray matter. These collaterals entering the gray matter from the dorsal tracts are conspicuous features of nearly all cross-sections of the spinal cord. The same disposition of cranial nerve-fibers, centripetally directed, was observed by Kölliker. In these subdivisions and collaterals of the sensory fibers given off at different levels in the cord and medulla oblongata, doubtless lies the anatomical explanation of simple and complex reflex actions and probably also of the simultaneous production of reflex action with consciousness of the stimulus producing it.

Ramón y Cajal also showed that in all probability Golgi's cell-type I differs from cell-type II only in the destination of their respective axons, that of the former ending in an arborization at a considerable distance from the cell-body, while that of the latter divides up near the cell-body, each being peculiarly adapted to the function required of it.

In this way is explained the more frequent occurrence of cells of type I which are found almost exclusively in paths uniting more or less distant portions of gray matter, and the finding of cells of type II only in gray matter, in which are found numerous cells, with their communications formed by the minutely branching axis-cylinder processes (dendraxons). Intermediate forms of axonic branching have been described, occurring in the spinal cord and in the cerebellum.

The more recently introduced methods, methods of staining nerve-tissue with methylene blue, either *intra vitam*, as suggested by Ehrlich, or *post mortem*, have confirmed largely the results obtained previously by other methods. They have perhaps given rise to greater uncertainty as to the ultimate anastomosis on the one hand, or relationship of contact on the other, between associated neurons. Leaving that point for the future to decide, the neuronal theory considers the nervous system, aside from its neuroglia, blood vessels and lymphatics, as made up of countless individual nerve-elements, or neurons. Each of these is a complete cell, and throughout life it is morphologically, and in a sense also physiologically, independent of every other neuron, establishing communication with other neurons only by contiguity, as the leaves of two trees may touch, without substance actually passing between them. The axon found in nerve-fiber, like the protoplasmic process (dendrite) found in gray matter, forms an integral part of a nerve-unit, with organic connection somewhere with a nerve cell, or cell-body. In higher animals, the conduction of nervous impulses usually proceeds along several neurons in one direction, superimposed upon each other, forming chains, each neuron of the chain being in a position to be affected by, and in its turn to affect, one or several other neurons. Though varying in detail of construction, all neurons show general similarity of form. "The nerve life of the individual, including all his reflex, instinctive and volitional activities, is the sum-total of the life of his milliard of neurons."

Fig. 277.



d. **The Neuronal Cell-body.**—Neurons, constituting as they do single body-cells, possess, like liver-cells or spleen-cells, certain general cell-characteristics, such as cytoplasm, nucleus and nucleolus, a fact which, however, does not explain their superiority in function over other cells. Chemical biology may some day indicate the essential differences. Within the last four years, the existence of a centrosome and centrosphere in nerve-cells taken from lower and higher animals has proved a still closer similarity between them and other cells. Whether the centrosome and centrosphere exist for any more important purpose than to aid in cell-division, is still doubtful. It has been demonstrated that they are found in cells that have lost all tendency to divide, which would suggest some further function presided over by them.

FIG. 278.

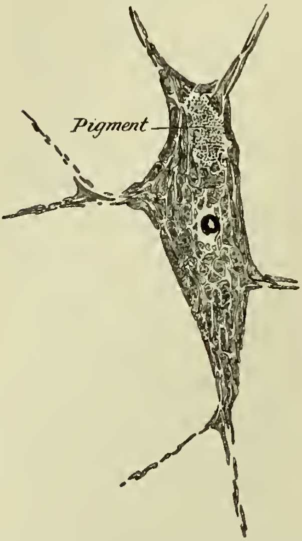


FIG. 279.

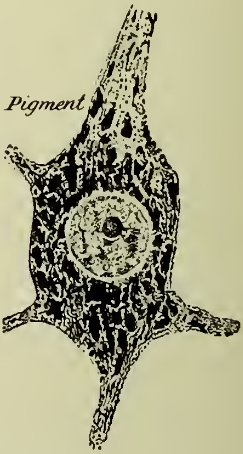
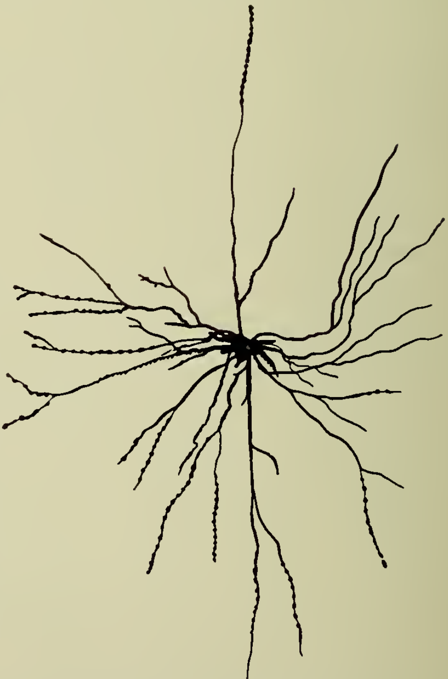
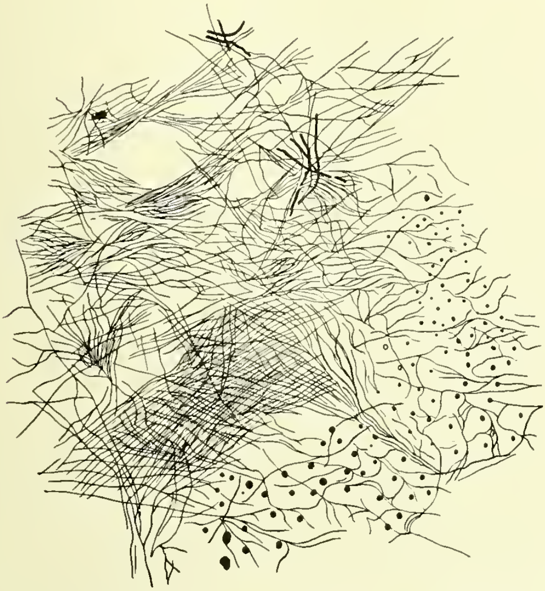


FIG. 280.



The cell-bodies of neurons vary in size from four to one hundred and thirty-five or more micro-millimeters in diameter. Many are of characteristic appearance, as for example, the unipolar cells of the spinal ganglia, the bottle-shaped cells of Purkinje in the cerebellum, and the pyramidal cells of the cerebral cortex. Among the smaller cells are the granules of the bulbus olfactorius and the small cells of the cerebellum, while many of the larger ones, as the multipolar cells of the ventral horns of the cord, and the cerebellar cells of Purkinje are distinctly visible to the naked eye. Figures 277–281 show the structure of a neuronal cell-body.

FIG. 281.



Figs. 277–281. *Neuronal cell-body.* Figs. 277 and 278, cells from the anterior horn of a human spinal cord. Fixed with alcohol and stained with methyl-blue; 279, ganglion-cell fixed with alcohol and stained with hæmatoxylin; 280, ganglion-cell from anterior horn of fœtal dog. (After an original preparation by RAMÓN Y CAJAL.) Prepared with Golgi's method. 281, neuroglia. (After an original preparation by WEIGART.) Neuroglia-fibers blue; axis-cylinders black. (After an original preparation by NISSL.) (Figure and description from the author's translation of EDINGER'S *Anatomy of the Central Nervous System.*)

(*e*) **The Dendrites.**—The dendrites, or protoplasmic processes, resemble more closely in appearance the cell-body itself than does the axon. Leaving the cell-body by broad thick bases, they divide and subdivide into numerous fine twigs, which end in free extremities, and these free ends, as has been stated before, communicate with the branches of other neurons only by entering into contact with the latter. The dendrites of one cell, as well as those of different cells, vary in length, and it has also been claimed that, under certain conditions, a given dendrite may lengthen or shorten, a theory of vast importance, if true, as explaining the "making" and "breaking" of nerve-currents, so to speak. In some cells one dendrite may be greatly developed, while the others remain small and slender. Enlargements along the course of the dendrites have been observed, although they may arise from artificial causes. The dendrites are seldom straight in their course, usually irregular in direction, in somewhat marked contrast to the axons. The branching of a dendrite may occur near to or at some distance from its origin at the cell-body. With some cells the dendritic tufts cover a surprisingly large area; in others they are relatively insignificant in extent. Again, from some cell-bodies the dendrites originate apparently from nearly every point in the cell-surface, whereas in others, a more or less considerable portion of this surface is smooth and unbroken. Some cells are called adendritic, from the apparent absence of dendrites; but with the axons of such cells there issue various branches, united at first with the axons, but soon leaving the latter and dividing in a manner characteristic of dendrites. They have been variously termed dendrites and axonic collaterals. The unipolar cells of the posterior spinal ganglia might be classed under this category, were it not that in the embryo, these cells are bipolar, and the two processes are merged into one at or a little before birth. The single dendrite of these cells is like an axon in so far as it is a medullated fiber coming from the periphery, whereas dendrites within the cerebro-spinal axis are devoid of myelin sheaths, as are the cell-bodies themselves.

The dendrites of certain nerve-cells are further characterized by numerous minute buds, short lateral branches with clubbed extremities, to which the name *gemmules* has been applied. They appear uniformly on the dendrites of the pyramidal cells and on those of Purkinje's cells, when treated with nitrate of silver. They are, in all probability, not artificial products, but their function has not yet been determined.

(*f*) **The Axons** differ in many ways from dendrites: (*α*) They leave their respective cell-bodies by narrow wedge-shaped beginnings, contrasting with the broad central ends of dendrites. (*β*) The dark bodies of Nissl found in the cell-body and its dendrites, after treatment with alcohol, are not found in the axon. (*γ*) The caliber of the axon varies less with its length than does that of the dendrites from the same cell, and it is usually maintained intact for some distance. This is true, even in the dendraxons of Golgi's cell-type II. (*δ*) The surface of an axon is smooth, its contour regular, and it pursues a fairly direct course, though not always the shortest one to its destination.

The length of an axon varies from a few millimeters to half the height of an individual. The longest ones are those of the motor paths, and are usually *monaxons, i. e.,* they form each the single axon from their respective cell-bodies. Most neurons are monaxonic; those of the posterior spinal ganglia may be called *diaxonic* from the division of their axons, soon after entering the cord (also called schizaxons), while there are found other nerve-cells giving off several axons, which are hence *polyaxonic.* These latter neurons are rare. Ramón y Cajal finds them in the sympathetic system, notably in Auerbach's and Meissner's plexuses. Neurons without axons (*anaxons*) are found in the bulbus olfactorius, retina, and in the baskets of Purkinje's cerebellar cells. The distal terminals of axons are usually branched and free. The branches may form an arborization around a single cell, or they may spread over a considerable area, thus establishing relationship with dendrites of a large number of neurons.

It perhaps seldom happens that the terminals of a given axon are in relationship with the dendrites of only one other neuron, but usually with many others, which explains Cajal's term "*avalanche conduction.*" Among the curious forms of axonic terminals observed may be mentioned the "climbing fibers" in the cerebellar cortex, the "discs" in Meissner's corpuscles and epithelial surfaces. But it must not be forgotten that many axons terminate in close contact with the cell-bodies of the secondary neurons, without the usual intervention of dendrites from the latter.

Axons of Golgi's cell-type I, are usually single and are generally, but not always, medullated. External to this myelin sheath is the neurilemma, which is wanting, however, within the cerebro-spinal axis. (See Fig. 59, p. 95.) The axons in the sympathetic system are non-medullated, but have a neurilemma. The medullary sheath, when present, is usually wanting near the cell-body, and also on the axonic terminals, even when these are within the central nervous system, or form motor end-plates.

(*g*) **Axonic Collaterals.**—By the aid of its *collaterals* a given axon enters into relationship which many nerve-cells, lying between its proximal and distal ends, a fact which explains complicated reflexes.

The number of collaterals which an axon possesses varies in different parts of the nervous system. Some, like those in the ventral horns of the cord, are without collaterals. In general it may be stated that those axons which course through the cerebro-spinal axis are provided with collaterals, while those in the peripheral nervous system are devoid of them, and when present, they are more numerous along that part of the axon near the cell-body (cytoproximal end) than beyond, in the cytodistal part. This leads us to suppose that in the spinal cord more collaterals are in the column of Burdach than in that of Goll, which is true; the latter fasciculus, made up of the cytodistal portions of axons which lower down in the cord occupy Burdach's column, is practically free from collaterals. The collaterals are usually medullated, and terminate in free ends, forming arborizations.

2. THE PHYSIOLOGY OF THE NEURON.

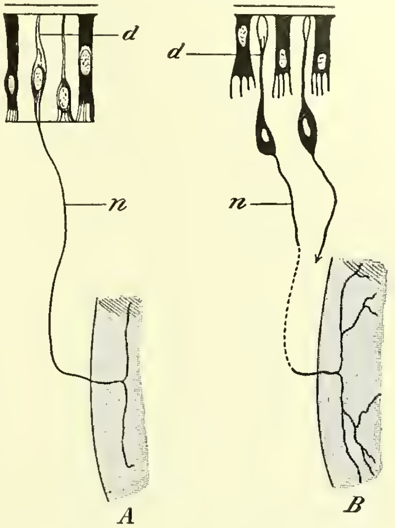
(*a*) **Cellulipetal and Cellulifugal Messages.**—Spontaneous activity is not a property of a nerve-cell; hence its function may, in a sense, be regarded as always called forth by some irritation external to the cell or its branches. This external irritation may be transmitted to it through some neighboring neuron or other structure, or it may arrive from some source more remote. In monaxons the impulse passes always away from the cell-body, hence is cellulifugal. By the splitting of the axon into its terminal fibers and fibrils is presented a good instance of the law of the multiplication of effect, as, for example, in the distribution of the terminal fibrils of a lower motor neuron among the muscle-fibers of its correlated muscle. Again, the stimulation of a single ganglion-cell in the retina is transmitted by its axons to several central cells in the anterior corpus quadrigeminum, or in the optic lobe. An apparent exception to, though in reality a confirmation of, the law of centrifugal function of axons is provided by the optic nerves, in which certain fibers functionate in a peripheral direction, their cell-centers, however, from which arise their impulses, being located in the corpus quadrigeminum. The explanation of this fact is not clear. It has been demonstrated that there are in the optic nerve, fibers, the stimulation of which causes contraction of the corresponding retinal cones. Others have associated them with the nutrition of the retina. But whatever their function is, it is exerted in conformity with the general law in a cellulifugal direction.

How is it with diaxons? In the spinal ganglia both the spinal and the peripheral processes have the characteristics of a true axis-cylinder, myelin sheath, terminal arborizations. But one is cellulipetal, the other cellulifugal, in action. Is the peripheral process, whose function is cellulipetal, an axon, or is it a transformed dendrite? Human ontogeny sheds no light on this question, but a study of the lower vertebrates proves the dendritic nature of these peripheral branches which, during the process of development, have become extended to a great length, and have assumed the histologic appearance of an axis-cylinder (see Fig. 282). In some of the invertebrates we find two types of peripheral sensory neurons, one with its cell-body in the central nervous apparatus, corresponding to the human type; the other represented by a cell-body and its dendrites in the integument, while its axon is directed centrally. The latter type corresponds to the peripheral nerve-cells of the human sense-organs and has been called "sense-cell (Sinneszelle)."

In all these forms of nerve-elements we find the law governing the reception and transmission of nervous impulses to be the same.

The cell-body receives the impulse either directly or through its dendrites, and transmits it through its neuraxon. We see, further, that as the dendrites provide for the reception of stimuli from a larger field than that represented by the cell-body itself, so, in many instances, is the discharge of these stimuli also accomplished over a large tract, through the medium of the axon. This occurs not only through its terminal filaments but by means of its numerous collaterals. In this manner the peripheral sensory neuron in vertebrates is in relation with all the levels of gray matter lying between its place of entrance into the spinal cord and its terminal branching in the nucleus of the posterior column to which it passes.

FIG. 282.



A, sensory epithelium of earthworm; *B*, of a snail. Note that the dendritic portion of the neuro-epithelial cells (*d*) is a single branch extending to the surface of the epithelial layer, and that the axon, neuraxon or neurite (*n*) extends from the cell body to the central nervous system or to some ganglion. (After RETZIUS.)

An analogous disposition of the olfactory neurons has been demonstrated. In addition to the collateral branches, so-called "lateral" fibrils, given off by the axonic stem before its sheath commences, are found. Their function is supposed to be receptive and not emissive, playing an important rôle in reflex phenomena. They have been called *axodendrites*.

(*b*) **The Dynamic Polarity of the Neuron.**—The idea of dynamic polarization given in the foregoing formed the subject of a heated controversy between different observers, and divided them into two schools. Of these Golgi headed those which denied the existence of such polarization, basing their opinion on the existence of globular cells (or adendritic cells) to be found in various parts of the nervous system. These cells were apparently provided with a single process, an axis-cylinder. From this they concluded that the dendrites, when present in a nerve-cell, did not participate in its nervous function, but were trophic organs.

The opposing school, including Van Gehuchten, R. y. Cajal, von Lenhossék, and others, insisted on the dendrites possessing a strictly nervous function. They demonstrated in these globular cells the existence of dendrites (axodendrites) joining the axis-cylinder and passing with it to join the cell-body. They also pointed to Golgi's cell-type II, in which the axis-cylinder process arises from the dendrites instead of from the cell-body, as proof of the anatomical and functional identity of the protoplasm in the dendrites and the cell-body. From this, further, they formulated the doctrine that an adendritic cell in fact could still exemplify the law of dynamic polarization, the cell-body itself receiving the stimuli directly, and not by any means through the axis-cylinder, as contended by Golgi.

(*c*) **Changes Within the Neuron During its Activity.**—As to the molecular movements and chemical changes occurring in the protoplasm of a neuron (cell-body and dendrites), while they doubtless present the physical basis of nervous manifestations, we have learned as yet but little. They are supposed to occur simultaneously with the respective phenomena, and to be propagated in the form of a wave (von Lenhossék).

The conditions necessary to *nervous conduction* and to automatic activity, or the *spontaneous discharge of nervous function*, coexist in the protoplasm of a neuron; the substance of the axon is only an organ of *transmission*.

Von Lenhossék has maintained that not all dendritiform processes are dendrites, but that they may be demonstrated at times to be modified forms of neuraxons. And while this does not combat the law of dynamic polarity, to which he subscribes, he differs somewhat from others of that school in his idea of what determines the order and the disposition of the dendrites. They believed these to be dependent on the functional associations of a neuron. Von Lenhossék believes this purpose could be served by fewer points of contact, and considers some of the dendrites as forming nutrient processes. A difference in the responsiveness must be imputed to the different dendrites of a neuron, as necessary to explain isolated conduction. The neuronal protoplasm is probably not always nor generally, equally excited by every irritant. One may regard its qualities of sensitive reaction as so regulated, that they respond only to certain forms of irritation, just as certain waves of sound excite vibrations in a cord of corresponding length, but not in other cords. This "corresponding susceptibility" may be physically represented by certain states of equilibrium and arrangements of the protoplasmic molecules. It would render unnecessary the supposition that the production of new associations in the psychic sphere provokes, as a material accompaniment, the formation of new dendritic branches, but that existing dendrites, hitherto idle, would supply the mechanism needed.

(*d*) **Function of the Nerve-fiber.**—The term nerve-fiber is used to designate not an anatomical unit, but one of those cell-branches which connect the neuronic cell-body with parts located at considerable distance from that body. The nerve-fiber may be dendritic, as in sensory nerves, or axonic. As stated above, when it is dendritic the substance of the nerve-fiber is protoplasmic, like that of the cell-body. But when it is an axon its structure is more fibrillated—a typical axis-cylinder, and it is rather to this structure that the term "nerve-fiber" applies. (Figs. 40, 41, 42 and 43, p. 70 *et seq.*, show the structure of typical nerve-fibers.)

Histologically, and in this restricted sense, we distinguish two kinds of nerve-fibers, (α) those which are surrounded by a medullary sheath, and (β) those which are devoid of such covering. The physiological importance of this sheath, or of its absence, is not well understood. It has been regarded as an insulating substance, implying a similarity between a nerve-fiber with the current passing through it and an electric wire with its current. The existence of unsheathed nerve-fibers, however, tends to disprove this hypothesis. We know that the medullary sheath is found generally on nerve-fibers which conduct sensory and motor impulses, extending from a point near their respective cell-bodies to the terminal branches. Certain cranial nerves, as well as those fibers belonging to the sympathetic system and conveying doubtless both afferent and efferent impulses, are either entirely devoid of such a sheath or have only a rudimentary one. Of the cranial nerves belonging to this category the olfactory and the pneumogastric form striking examples. In general it may be accepted that those efferent fibers which arise from centers in the cerebrospinal axis that are not under voluntary control are naked (Remak's fibers). Ontogeny teaches that medullated nerve-fibers acquire their medullary sheaths at different stages of development, the time being in close relationship with the developing function of the fibers. This function is a single one, the conduction of nervous impulses. Each fiber performs its function in one direction only, and that is determined in the beginning, when the neuron of which the fiber is a part puts forth its branches, to establish communication with its surrounding structures.

(*e*) **Function of End-organs.**—At the peripheral extremities of the teleneurons we often find specialized structures forming a part of the neuron itself, or in close relationship with it. These structures are known as end-organs. In motor neurons they take the form of end-plates closely applied to the muscle-cells, and offer the medium of communication of impulse, resulting in a change of form of the muscle cells. (See Fig. 38, p. 69.) In sensory neurons they vary according to the kind of sensation served (see chapter on special senses).

In this connection the question naturally arises, what determines the quality of impulse traversing a given neuron? Is it dependent on the cell-body, the dendrites, the neuraxon, or the end-organs, either separately or collectively? Different forms of stimuli applied to any part of a nerve-trunk or its center produce but one result, and that result depends apparently on the end-organ. If it be a motor nerve, motion in the respective muscle results. If it be a sensory nerve, the sensation usually excited by the nerve is experienced. Apparently, therefore, the nature of the impulse need not vary at all, wherever the neuron may be located or whatever may be the resultant sensation or manifestation, but at the terminus of the conducting path the impulse produces a result of a character dependent on the end-organ or end-connections.

Experiments have proved that an isolated nerve conducts equally well in one direction as in the other, and while the mechanical, chemical and electric stimuli, used in the experiments, may be neither identical with nor even similar to the natural excitants of nervous impulses, it is perhaps less important to know the nature of the impulse received by a neuron than it is to define its power of transmitting it further. For example, in a nerve-muscle preparation stimuli of various kinds when applied to the nerve produce contraction in the muscle. Manifestly here the end-plates are of prime importance as constituting the connection between nerve-fiber and muscle-fiber. And this suggests the idea that, for the efferent neurons, at least, the end-plates alone determine the quality of the nervous impulse. This is comparable with the various recording instruments that may be attached to an electric wire. The agent is the same, but the effect varies with the receiver used. In the peripheral sensory neurons, however, there seem to be special adaptations for the reception of stimuli, mechanical, chemical, etc. Thus in the skin mechanical and thermal stimuli are most effective. In the nasal mucosa and the taste-buds are found end-organs adapted to the reception of chemical stimuli.

From these considerations it appears that, while nervous impulses are excited differently according as the sensory end-organs (including, of course, those placed deep in the tissues as well as the superficial ones) are adapted to receive impressions, and while, further, the externalization of nervous energy, manifested by motion, secretion, nutrition, etc., depends largely on the peripheral end-organs, the character of nervous impulses never varies and may be identical in all instances.

(*f*) **Effect of Structural Modification on the Function of the Neuron.**—Comparative anatomy as well as human pathology shows the adaptation of the conducting paths to the functional requirements. In those vertebrates which have either rudimentary or undeveloped anterior or posterior extremities, the corresponding nerve-trunks and spinal roots are diminutive. After amputation of a limb its proper nerves with their extensions into the cord undergo a degeneration from disuse in proportion to the part lost.

(*g*) **Effect of Mutilation upon the Neuron.**—The cell-body of the neuron sustains an important relation to the nutrition of the neuron as a whole. The axon and dendrites are dependent upon the cell-body for their trophic supply. When a peripheral nerve-trunk is divided the distal portion dies because the sensory fibers are cut off from the posterior spinal ganglia, where their cell-bodies are situated; and the motor fibers die because they are cut off from their cell-bodies in the ventral horns of the spinal cord. This form of degeneration is called *Wallerian*, after the law of Waller, who first discovered it. But another form of degeneration takes place in the part still attached to the cell-body—a slow degeneration which ascends toward the cell-body. This is called *retrograde degeneration.*

The amputated portion of an axon changes profoundly and rapidly. The myelin is broken up and absorbed, the process itself disappears more or less completely, and finally not a vestige of nerve-structure may remain. The stump of axon remaining behind also degenerates slowly, though not so completely.

(*h*) **Postnatal Neuronic Development.**—Constituting what may be designated as a third function, although it is merely a property by which the first one, enumerated above, is more extensively operative, is the ability on the part of certain neurons, notably those of the cerebral cortex, to develop additional dendrites, to form new relationships with cells that hitherto were foreign. On this hypothesis rests the enormous development of the cerebrum of an individual undergoing education. As such development depends largely upon the extensive and diverse correlation of existing cells and centers, it will readily be seen how great is the demand for new dendrites. Possibly also new axons, if not entire neurons, are required and furnished in a manner as yet unknown.

It is further stated that newly proliferated dendrites may soon again disappear, after the particular object served by them is no longer required. This may be a species of atrophy from disuse, but it is sometimes likened to amœboid movement, the cell-protoplasm being protruded and withdrawn according to the need.

The functions of the single neuron indicate those of systems of neurons, which may be considered as a reinforcement of the former. In addition, however, by reason of the numerous associations existing between neurons of one system, and those of other systems, intricate and complex actions, expressions of nervous activity, are possible. In studying these relationships more closely, an additional power of some neurons over others is found, viz.: the power of restraining, or inhibiting their action. A familiar example of this is met with in the two sets of neurons making up the motor chain from the cerebral center to the muscle. Of these two sets of neurons, the upper (archineurons) restrain the lower (teleneurons) in their function. This is shown by the phenomenon of muscle-reflexes, which are present only when the teleneurons are functionally intact. In health these reflexes are but moderately active, owing to the inhibition of the archineurons. If through disease of the latter, the inhibition is withdrawn, then the teleneurons are freer to act, and increased reflexes are noted.

B. THE PHYSIOLOGY OF THE SPINAL CORD.

Physiologically the spinal cord must be considered as extending beyond its upper anatomical limits. Indeed, a better term were "cerebro-spinal cord," to indicate that the cerebral stem is merely a continuation of the spinal. Usage, however, sanctions the term spinal cord, and it will be employed here in its extended sense.

1. THE SPINAL CORD AS A CONDUCTOR OF NERVOUS IMPULSES.

In its function of *conducting nervous impulses* the spinal cord differs from a peripheral nerve only in its complexity. Essentially its fibers, while forming large tracts, are similar to those of the peripheral nerves in function. But we find here, in addition, collections and chains of cell-bodies, toward and from which the fibers conduct impulses. We have already seen that the cell-body of a neuron is a trophic center for its branches, and serves to receive, and possibly modify, impulses coming to it, and to discharge them through the axon. Each of the cell-bodies found in the spinal cord in such numbers represents a neuron, just as each one in the posterior spinal ganglia does, and as, indeed, every cell-body in the nervous system. And while they may be regarded as centers, they are in one sense only mid-stations in the course of an impulse through a neuron.

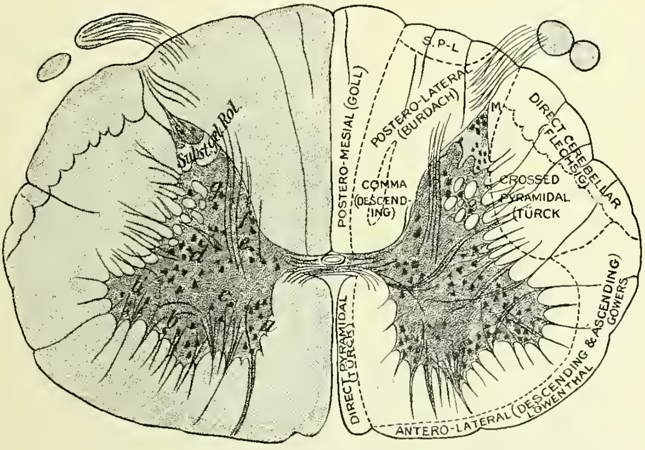
With these considerations always before us, let us endeavor to learn more of the conductive functions of the cord. And first of all comes the fact that all impressions received from the outside world as well as those coming from the structures of the body itself, and all impulses resulting in motion, secretion or other manifestation of nervous energy, must pass through the cerebro-spinal cord. These may be summed up as *afferent impressions* and *efferent impulses.* And the center, toward which the one class goes and from which the other departs, the mental organ, made up also of neurons, is for the individual the center of the universe, where are received his impressions of everything external to his body as well as of the changing conditions of the body itself, and from which emanate all his voluntary and involuntary acts.

a. The Course of Sensory Impulses.

Among the efferent impressions must be placed all such as arrive through our senses, general and special; in addition, subconscious information of the changing conditions of insensible portions of the body.

In tracing the paths taken by these impressions through the cord, ontogeny and morbid anatomy have greatly furthered our knowledge. By means of a series of examinations of the nervous system corresponding in time to newly developing nervous phenomena we learn that new tracts of nerve-fibers develop from time to time. And evidences of degeneration of these various tracts, furnished by morbid anatomy, together with the losses or disturbances of function previously noted clinically have aided us in establishing clearly the courses followed by such impulses.

Fig. 283.



In this manner it has been demonstrated that, in general, afferent impulses enter the cord through the posterior roots and ascend through its posterior and lateral tracts, while efferent impulses on the other hand descend through the anterior and lateral tracts of the cord. (See Figs. 60 and 61, pp. 97 and 98.)

Under the head of sensations,—impressions received through the senses,—we distinguish *common* and *special sensations.* The former include tactile, pain, thermal and muscular sensations; the latter, visual, olfactory, auditory and gustatory sensations.

Tactile, pain, thermal and muscular impressions arrive at the cord through the sensory teleneurons contained in the posterior spinal roots and their analogues in the cranial nerves, the various fibers combined in the nerve-roots. Not until after their entrance into the cord are they separated from each other and follow different tracts. These tracts are not all definitely known. The fibers subserving muscular sense enter the postero-lateral columns directly and ascend in them, being pushed inward by newly arrived fibers until they come to occupy the postero-median column. Ascending to the medulla oblongata they enter into an arborization with dendrites from the cell-bodies of the nuclei graciles and cuneati, whose axons, in turn, lead into the cerebellum.

Fig. 284.

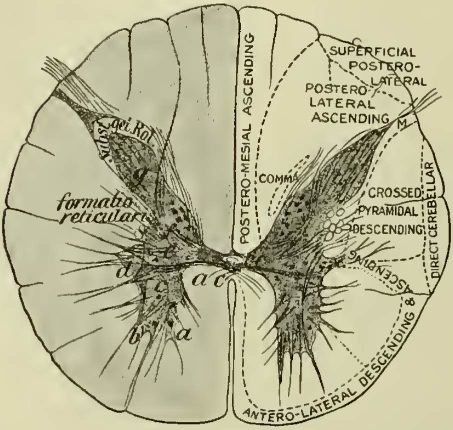
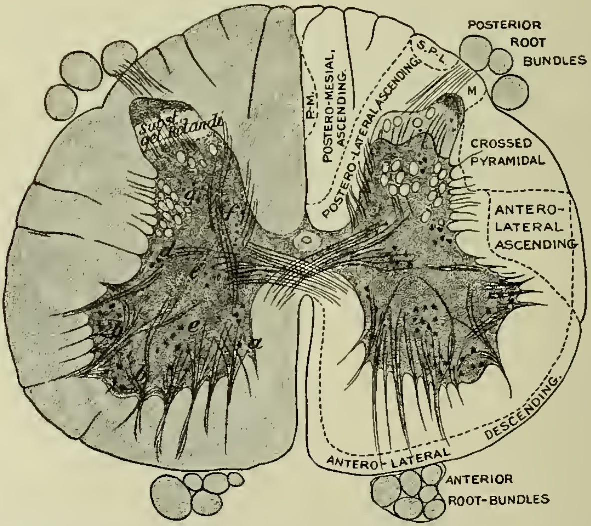


Fig. 285.



Sections of human spinal cord. Fig. 283, the lower cervical region.
Fig. 284, the mid-dorsal region.
Fig. 285, the mid-lumbar regions, showing the principal groups of nerve-cells, and on the right side of each section the conducting tracts as they occur in the several regions. (Magnified about seven diameters.)
a, *b*, *c*, groups of cells of the anterior horn ; *d*, cells of the lateral horn ; *e*, middle group of cells ; *f*, cells of Clarke's column ; *g*, cells of posterior horn ; *c*, *c*, central canal ; *a.c.*, anterior commissure. (SCHAEFER.)

The fibers which conduct pain and thermal sensations are probably closely associated with each other. From the prominent part played by the loss or perversion of these two forms of sensation early in the history of cases of syringo-myelia, in which the spinal gray matter is usually first affected, we are justified in concluding that the fibers conducting these impressions, soon after entering the cord, pass into the gray matter and these arborize with secondary neurons. About the latter much uncertainty prevails. By some their axons after crossing over in the commissure are thought to extend upward in the antero-lateral ascending (Gower's) tract. (See Figs. 283–285). By others they are conceived as forming the first in a series of short loops lying in the lateral marginal zone and dipping at short intervals into the gray matter to arborize there with the next higher neuron of the series, and so on up to the medulla.

The difficulties encountered in determining the course of pain and thermal impressions after they quit the teleneurons are almost if not quite insurmountable. Even in the peripheral nerves a lesion causing more or less permanent motor loss often produces only passing sensory disturbances. In the higher links of the chain it is possible that lesions may be compensated for by more numerous inter-communications, rendering it more difficult by a single lesion entirely to interrupt the path. Experiments on lower animals have not advanced our knowledge materially in this matter, owing to uncertain interpretation of sensations experienced by them.

In tracing the path of tactile impressions through the cord similar difficulties are encountered. They are believed to follow the course of muscular sensation, at least in part, crossing over in the posterior commissure to ascend in the ventral portion of the posterior columns. Some tactile fibers, however, decussate and ascend in the antero-lateral ground-bundle along with the pain fibers.

All of these fibers conducting sensory impressions coming into consciousness pass up through the lemniscus, or fillet, of the medulla, pons, mid-brain, and cross to the internal capsule, where they are situated posteriorly, and radiate to the Rolandic areas, occupying portions of these areas corresponding to the motor fields.

b. The Course of Motor Impulses.

Motor impulses arising in contiguous cells in the same areas, descend through the pyramidal tract by the neuraxons of these cells. They extend through the internal capsule, the crusta, pons, and medulla, lying ventral to the fibers we have just been considering. In the lower part of the medulla the larger part of these pyramidal fibers decussates and descends in the opposite lateral column, while a smaller number descends in the anterior column of the same side. The latter, just before entering into communication with their secondary neurons, pass over through

FIG. 286.

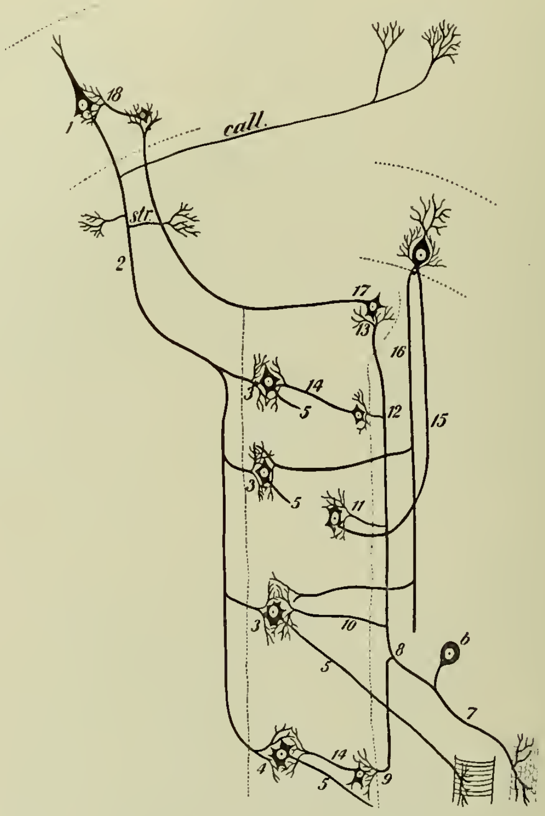


Diagram showing the probable relations of some of the principal cells of the cerebro-spinal system to one another. 1, a cell of the cortex cerebri; 2, its axis-cylinder or nerve process passing down in the pyramidal tract, and giving off collaterals, some of which, 3, 3, end in arborizations around cells of the anterior horn of the spinal cord, the main fiber having a similar ending at 4; *call.*, a collateral passing to the corpus callosum; *str*, another passing to the corpus striatum; 5, axis-cylinder process of anterior cornu-cell passing to form a terminal arborization in the end-plate of a muscle-fiber, *m*; 6, a cell of one of the spinal ganglia. Its axis-cylinder process bifurcates, and one branch, 7, passes to the periphery to end in an arborization in the sensory surface, *s*. The other (central) branch bifurcates after entering the cord (at 8), and its divisions pass upwards and downwards (the latter for a short distance only); 9, ending of the descending branch in a terminal arborization around a cell of the posterior horn, the axis-cylinder process of which, again, ends in a similar arborization around a cell of the anterior horn 10, a collateral passing from the ascending division directly to envelop a cell of the anterior horn; 11, one passing to envelop a cell of Clarke's column; 12, a collateral having connections like those of 9; 13, ending of the ascending division of the posterior root-fiber around one of the cells of the posterior columns of the bulb or medulla oblongata; 14, 14, axis-cylinder processes of cells of the posterior horn passing to form an arborization around the motor cells; 15, a fiber of the ascending cerebellar tract passing up to form an arborization around a cell of the cerebellum; 16, axis-cylinder process of this cell passing down the bulb and cord, and giving off collaterals to envelop the cells of the anterior horn; 17, axis-cylinder process of one of the cells of the posterior column of the bulb passing as a fiber of the fillet to the cerebrum, and forming a terminal arborization around one of the smaller cerebral cells; 18, axis-cylinder process of this cell, forming an arborization around the pyramid-cell, 1. (SCHAEFER.)

the anterior commissure of the spinal cord, and in the opposite anterior horn arborize with dendritic fibers from cells in that horn. To other cells in this location come the fibers of the crossed pyramidal tract and form with them similar arborizations (see Fig. 286). The lower neurons send out their axons as motor fibers of the anterior roots and peripheral nerves to the muscles, where they end in the familiar "plates" in contact with the muscle-fibers. It is scarcely necessary here to call to mind the fact that two neurons constitute the motor chain from the cerebral cortext to any muscle remote or near, while the sensory impressions arrive at the sensorium only after several additional interruptions. The thalamus opticus, and nucleus caudatus contain cell-stations for some of these fibers, and the anterior corpora quadrigemina and the external corpora geniculata, for fibers of the optic tracts.

It is important to remember that sensory impressions, entering into consciousness (perception), must do so by way of this devious and complex path, and motor impulses, resulting from their perception, must descend by the two-link chain described. Thus a circuit is formed, whereby conscious sensation results in voluntary muscular contraction.

2. THE SPINAL CORD AS A REFLEX CENTER.

By virtue of its conductive function, which is only slightly differentiated from that of peripheral nerves, the spinal cord possesses another function, distinctive in itself. A sensory impression entering the cord by the teleneurons, which we have been studying, instead of ascending to the cerebral cortex and becoming an element of consciousness, may be conducted by collaterals of the sensory teleneuronic axons direct to the motor teleneurons arising in the anterior horns of the cord. This is a short circuit and forms the path taken by those subconscious sensations which arouse involuntary muscular contraction, giving us the phenomenon called *reflex action.* In some conditions of disease and in certain forms of intoxication, every voluntary muscle of the body can be made to contract reflexly, in health comparatively few respond, while in other diseased conditions reflex action is diminished or entirely lost.

a. Reflex Action.

1. **General Considerations.**—Before considering the more important reflexes of the body, let us endeavor to account for the fact of increased reflex action in one disease and loss of reflex action in another. Recall, first, that true reflex action is involuntary motion resulting from unperceived sensation. Now let us suppose the sensation to be perceived; that is to say, it ascends to

the cerebral cortex. Two things may result: either a voluntary action superseding the reflex, or a voluntary inhibition. If the latter take place, an impulse descending the motor archineurons interferes with the reflex activity of the teleneurons, and no reflex occurs. From this it is clear that the only restraint exercised over reflex activity is exerted through the motor archineuron. Suppose this to be interrupted by a lesion anywhere in its path. The inhibition is withdrawn, the lower neuron is unhindered, and heightened reflex action is observed.

The mere presence of reflex action is indicative of the fact that the motor and sensory teleneurons with their collateral branches of communication are intact. Loss of reflexes implies an interruption to this circuit, called the reflex arc. And as the arc is composed of a sensory neuron and a motor neuron, the lesion may be located in either one or the other. If there be a lesion of the motor arm of the reflex arc, not only is reflex action lost but also voluntary action, and complete paralysis is present in the part. If reflex action alone is lost, while voluntary action is possible, the lesion must be in the sensory arm of the reflex arc. In the latter case other sensory disturbances are to be looked for.

Reflex action constitutes in its varied forms a most important part of the life of every animal. In the lowest organisms it is of paramount value, the relations existing between stimuli received from the environment and the reactions thereto on the part of the animal making up the sum of its existence. Ascending the scale of development, reflex actions multiply in number and diversity, and there is gradually evolved an additional higher form of nerve-center than that concerned in reflex action, one which provides for the storing up of impressions, for comparisons between them, and for all the phenomena of psychic activity.

But in the presence of this more recently developed, higher nerve-center, the subsidiary centers of reflex action have not become less important for the life of the individual, even if somewhat overshadowed. In human physiology, the subject here considered, we find reflex action forming the basis of the vegetative functions, so-called, and so well developed, indeed, that in the absence or loss of the higher psychic centers, life still is continued by reason of the activity of the reflex centers in the medulla spinalis and oblongata. Under the chapters on respiration and circulation (*q. v.*) it will be found that these vital functions depend on the condition of aëration of the blood. That provides the stimulus to the respiratory and circulatory centers in the bulb, and by reflex action resulting in the necessary contraction and relaxation of the muscles of the chest-walls and the heart, these phenomena recur in a continuous succession of cycles, and so life is prolonged.

2. **Purposeful Character of Reflex Action.**—In observing results of experiments on animals the purposeful character of the reflexes is striking. In all reflex movements, whether of a simple or complex nature, the response is in proportion to the strength and nature of the stimulus, that is, the afferent impulse. Reflex movements may be divided into the three following groups: (*a*) Simple or partial reflexes. (*b*) Extensive incoördinate reflexes or reflex spasms. (*c*) Extensive coördinated reflexes.

(*a*) THE SIMPLE OR PARTIAL REFLEXES are characterized by the fact that stimulation of a sensory area discharges movements in one muscle only, or at least in one limited group of muscles, *e. g.*, contact with the conjunctiva causes closure of the eyelids.

(*b*) THE EXTENSIVE INCOÖRDINATE REFLEXES OR REFLEX SPASMS: These movements occur in the form of clonic or tetanic contraction in individual muscles, or all of the muscles of the body may be implicated.

Causes.—A reflex spasm depends upon a double cause: (*α*) The gray matter of the spinal cord may be in a condition of exalted excitability so that the nervous impulse after having reached the center, is easily transferred to the neighboring centers. This excessive excitability is produced by certain poisons, more especially by strychnin, brucin, caffein, atropin, nicotin, carbolic acid, tetanin. The slightest touch applied to an animal poisoned with strychnin is sufficient to throw the animal at once into spasms. Pathological conditions may cause similar results, as in hydrophobia and tetanus. On the other hand, the central organ may be in such a condition that extensive reflexes cannot take place; thus in the condition of apnœa the spasms that occur in poisoning with strychnin do not take place.

(*β*) Extensive reflex movements may also take place when the discharging stimulus is very strong. For example, this condition occurs in man when in great pain; thus, intensive neuralgia may be accompanied by extensive spasmodic movement—Tic douloureux.

Strychnin is the most powerful reflex-producing poison known. When a large dose is given to an adult the lower jaw becomes immovable, the neck rigid, the pupils dilate, the reflexes are heightened so that the muscles contract spasmodically and painfully, resulting in paroxysmal attacks of tonic contraction of the extensor muscles of the body, in which the patient assumes the position of opisthotonos. If the heart of a frog be ligatured and the poison afterwards applied directly to the spinal cord, reflex spasms are produced, proving that strychnin acts upon the spinal cord. We can prove that strychnin does not produce spasm by acting on the brain, muscle or nerve. Destroy the nerve high up and inject a small dose of strychnin into the dorsal lymph-sac; in a few minutes all the muscles of the body, except those supplied by the divided nerve will be in spasms, showing that although the poisoned blood has circulated in the nerves and muscles of the legs, it does not act on them. Destroy the spinal cord and the spasms cease at once.

Summation of Stimuli: By this term is meant that a single weak stimulus, which in itself is incapable of discharging a reflex act, may if repeated sufficiently often produce this act. The single impulses are conducted to the spinal cord in which the process of summation takes place. It is believed by some to be extremely probable that all reflex acts are due to the repetition of impulses in the nerve centers,—summation of stimuli.

(*c*) EXTENSIVE COÖRDINATED REFLEXES are due to stimulation of a sensory nerve causing the discharge of complicated reflex movements, in whole groups of different muscles, the movements being powerful in character. Example: the protective movements of pithed or decapitated frogs. If a drop of a dilute acid be applied to the skin of such a frog, it strives to get rid of the offending body and it generally succeeds. Thus when a drop of acid is placed on the right flank of a brainless frog, the right foot is almost invariably used to rub off the acid. If the right foot be cut off or otherwise hindered from rubbing off the acid the left foot is, under exceptional circumstances, used for this purpose. This at first sight appears like an intelligent choice; indeed so purposeful are these acts and the actions of groups of muscles so adjusted to perform a particular act that Pflüger regarded them as directed by and due to consciousness of the spinal cord. If many instances occurred where evidences of a variable automatism which we call volition, were manifested by the cord, we should be led to believe that the choice was determined by an intelligence. But as has been abundantly observed, a frog in which the brain has been removed having only the spinal cord, makes no spontaneous movement.

Vicarious reflex movements are observed in mammals, though not to such an extent as in frogs. In dogs in which partial removal of the cerebral hemispheres has apparently heightened the reflex excitability of the spinal cord, the remarkable scratching movements of the hind leg which are called forth by stimulating a particular spot on the loins or the side of the body are exerted by the leg of the opposite side if the leg of the same side be gently held. In this case the vicarious movements are ineffectual, the leg not being, as in the case of the frog, crossed over so as to bear on the spot stimulated and this therefore cannot be considered as an act of intelligence. The mechanical nature of reflex action can be further illustrated. If a flame be applied to the side or part of the body of an eel, the body is moved away from the flame. If the bodyof a decapitated snake is brought into contact at several places with an arm or stick, complex reflex movements are excited, the effect of which is to twine the body around the object. A decapitated snake will with fatal readiness twine itself around a red-hot iron.

In the reflex acts which have been under consideration we have observed that the resultant movements are coördinated, and not only are many distinct muscles brought into play but certain definite relations between the contraction of each muscle and the contraction of other muscles sharing in the movements are maintained. In the absence of coördination the movements would become irregular and ineffectual. There is reason to believe that this coördination of voluntary muscular movement takes place in the part of the spinal cord which carries out the movement and not in the brain, though under normal conditions the latter may be conscious of the whole movement, including its coördination. As may be inferred from what has already been said, the characters of a reflex movement are dependent on the intrinsic condition of the cord. The action of strychnin, already alluded to, is an instance of an augmentation of reflex action. Conversely by various influences of a depressing character, as by various anæsthetics or other poisons, reflex action may be lessened or prevented. So also various diseases may so affect the spinal cord as to produce either increased reflex excitability so that a mere touch may produce a violent movement, or diminished reflex excitability so that it becomes difficult or impossible to call forth a reflex action.

Coördinated reflexes may occur in man during sleep and during pathological conditions. Reflexes are more easily and more completely discharged when the specific end-organ of the afferent nerve is stimulated than when the trunk of the nerve is stimulated in its course; by gently tickling the skin a reflex act is more readily evoked than by a strong stimulus applied to sensory nerve.

3. **The Time Required for Reflex Actions.**—In the frog, deducting the time taken in the transmission of impulses along nerves, the time consumed in the cord (reflex time) varies from 0.008 to 0.015 second; if the reflex crosses to the other side it is one-third longer. It is lessened by heat, and by the influence of a strong stimulus.

4. **Inhibition of the Reflexes.**—Within the body there are mechanisms which can suppress or inhibit the discharge of the reflexes, and they may therefore be termed mechanisms inhibiting the reflexes.

(*a*) VOLUNTARY INHIBITION.—The observations of every-day life teach that reflex acts can be inhibited to a certain extent by action of the will. The eyelids may be kept open when the eyeball is touched; movement of a part may be arrested when the skin is tickled. If, however, the stimulus be strong and is repeated with sufficient frequency, the reflex impulse ultimately overcomes the voluntary effort. Inhibitory acts are not all similar in character; for example, when we voluntarily stop the muscular acts which result from tickling the sole of the foot, we achieve this by throwing into action an opposing group of muscles, but it is doubtful whether inhibition is to be wholly explained as a matter of muscular antagonism. When the brain of a frog is removed and the effects of a shock have passed off the reflex excitability of the animal is found to be increased. This suggests the idea that in the intact nervous system the brain is exerting some inhibitory influence on reflex actions. If a frog from which the cerebral hemispheres have been removed (the optic lobes, bulb, and spinal cord being left intact) be tested by applying a drop of acid on its skin, it will be found that the reflex excitability is increased. If, however, the optic lobes be stimulated by applying a crystal of salt the reflex acts are prolonged or suppressed. Similar results may be obtained by stimulating in mammals the corpora quadrigemina, which bodies are analogous to the optic lobes of frogs.

(*b*) BEYOND VOLUNTARY INHIBITION are those reflex movements which cannot at any time be performed voluntarily. Thus erection, ejaculation, parturition and the movements of the iris are neither direct voluntary acts, nor can they, when they are excited reflexly, be suppressed by the will. It will be recalled that the action of such nervous centers as the vaso-motor and respiratory may be either inhibited or augmented by afferent impulses. The micturition center in the mammal may be inhibited by impulses passing downward to the lumbar cord from the brain or upward along the sciatic nerves. In the case of dogs whose spinal cord has been divided in the thoracic region, micturition set up as a reflex act by simple pressure on the abdomen, is at once stopped by sharply pinching the skin of the leg, and it is a matter of common experience that in man micturition may be suddenly checked by an emotion or other cerebral event.

(*c*) UNCONSCIOUS CEREBRAL INHIBITION is a prominent feature of reflex action. Strong stimulation of a sensory nerve inhibits reflex movements. If the toes of one foot of a frog are dipped into dilute sulphuric acid at a time when the sciatic of the other leg is being powerfully stimulated with an interrupted current the period of incubation of the reflex act will be found to be much prolonged and in some cases the reflex withdrawal of the foot will not take place at all; and this holds good not only in the complete absence of the optic lobes and bulb, but also when a portion of the spinal cord, sufficient to carry out the reflex action in the usual way, is left. The brain does, it is apparent, act as an inhibitory organ, but we must not draw too closely upon the inhibitory cardiac mechanism as analogous. In the mechanism of cardiac inhibition we have to do with fibers whose exclusive duty it is to act under control of the center in the medulla, as the brake mechanism of the heart. In the present state of our knowledge the fact must suffice that experiments on animals show that the brain may inhibit particular spinal reflex movements, but also habitually exercises a restraining influence on the reflex activity of the whole cord, though we are unable to state exactly how the inhibition is carried out.

b. The Reflexes.

From the inherent forms of reflex action down to the simplest muscular contraction following unperceived stimulation the human individual presents numerous gradations. By their functions, normal or deranged, they reveal the actual conditions of the nerve-elements composing their respective reflex-arcs. Among them are differentiated the superficial or cutaneous reflexes, the deep or tendon-reflexes, and the organic or visceral reflexes.

1. **Superficial Reflexes.**—(*a*) PLANTAR; elicited by stroking or scratching the sole of the foot, which causes attempts to withdraw the foot from the source of irritation.

(*b*) GLUTEAL; a contraction of the gluteal muscles *en masse* when the buttock is gently pricked or scratched.

(*c*) CREMASTERIC; when the thigh is irritated on its inner surface by grasping, stroking, scratching, etc., the homolateral testicle is distinctly retracted.

(*d*) ERECTILE REFLEX OF PENIS; produced by gentle friction of the glans penis, especially of the frænum, resulting in turgidity of the organ and erection. Its analogue in the female pertains to the erection of the clitoris.

(*e*) ABDOMINAL; consisting of a retraction of the anterior abdominal walls when the skin is slightly irritated.

(*f*) MAMMARY; in women, a retraction of the epigastrium when the mammary region is tickled.

(*g*) PALMAR; corresponding to the plantar, usually less developed than the latter.

(*h*) LARYNGEAL; irritation of the lining of the larynx, as also of the bronchi, produces coughing.

(*j*) PHARYNGEAL; attempts to extrude contents of the pharynx, even to the point of vomiting, when the fauces or lining of the pharynx is stimulated.

(*k*) NASAL; causing sneezing when the nasal mucous membrane is irritated.

(*l*) CONJUNCTIVAL; closure of the eyelid when anything foreign touches the conjunctiva or the eyelashes.

2. **Deep Reflexes.**—(*a*) *Tendo-Achillis Reflex.* When the ex-

tended leg is supported at the knee, the hand pressing firmly against the ball of the foot, a tap on the tendo-Achillis causes contraction of the gastrocnemius and soleus, and the heel is jerked up. This reflex may be present or absent in health.

(*b*) ANKLE CLONUS.—If the half-extended leg be supported at the knee, and the ball of the foot be suddenly pressed up, putting the tendo-Achillis on a stretch, in certain instances there results a series of clonic contractions of the calf-muscles with consequent alternate extension and flexion of the foot, which continues as long as the pressure is maintained on the ball of the foot and ceases as soon as the foot is released from pressure. It is probably never present in health.

(*c*) PATELLAR REFLEX (knee-jerk).—When the thigh is supported by the hand or by being crossed over the other thigh, and the leg is flexed at the knee, thus securing relaxation of the quadriceps extensor, a tap on the tendon just below the patella causes the leg to be suddenly extended. This reflex is normally present, but its exaggeration and its loss are both indicative of disease.

In conditions of exaggerated knee-jerk, if the hand be applied above the patella, pressing it down with a sudden movement, sometimes a clonic contraction of the quadriceps occurs and the patella is alternately raised and lowered. This is the *patellar clonus*.

(*d*) TRICEPS REFLEX (elbow-jerk).—This is analogous to the knee-jerk and is elicited by supporting the arm in the hand, on the examiner's knee, or by leaning on a table, the forearm being somewhat flexed, and then tapping the triceps tendon just above the olecranon. In health it may be absent or present. Its exaggeration is indicative of disease.

(*e*) With the arm in the foregoing position tapping the supinator and extensor muscles of the forearm often elicits contraction of them, with corresponding movements.

(*f*) BICEPS REFLEX.—If the flexed forearm be supported at the elbow, the wrist slightly flexed and also supported, tapping on the tendon of the biceps sometimes causes contraction of that muscle.

(*g*) WITH the arm in the position last described, tapping the pronator and extensor muscles of the forearm causes at times contraction of them and movements of the forearm, hand and fingers accordingly.

(*h*) INFERIOR MAXILLARY REFLEX.—If the mouth be opened and a flat instrument resting on the lower teeth be tapped, sometimes the jaws shut by reflex movement.

3. **Organic Reflexes.**—Under this head are included many of the functions of different organs of the body on which the well-being of the organism as a whole depends, some of them indeed

being of vital importance. Like the superficial and deep reflexes they are expressed by muscular activity, but unlike them usually the synergic function of several groups of muscles is required for their execution.

I. *The Alimentary Tract.*

(*a*) SUCKING.—When the mother's nipple is placed in the mouth of a newborn infant and a few drops of colostrum tasted by it, there ensues a form of peristaltic, vacuum-producing movement of the tongue and lips, which at first is probably reflex in its nature.

(*b*) DEGLUTITION.—The presence of food in the back part of the mouth and in the pharynx brings on successive dilatations and contractions in the segments of the œsophagus from above downward, constituting the act of swallowing. Only the initial part of this act is under voluntary control. The rest is purely reflex.

(*c*) GASTRIC MOVEMENTS.—These are induced by the presence of food in the stomach, and, as is well-known, serve as an important factor in gastric digestion. Closely associated with it and yet distinct from it is

(*d*) THE PYLORIC REFLEX, by virtue of which the contents of the stomach are retained in it until gastric digestion is complete. It consists of a firm contraction of annular muscle-fibers, and of a subsequent relaxation of these fibers permitting the stomach contents to pass into the duodenum.

(*e*) THE INTESTINAL MOVEMENTS.—These are perhaps not to be disassociated from those of the stomach, which they resemble at least to some extent. They are, too, similarly caused by the presence of the ingested food in them.

Whether a separate reflex act, or accomplished by the aid of duodenal peristalsis, the emptying of bile from the gall-bladder into the bowel is probably reflex. The presence of muscle-fibers in its walls would point to this.

(*f*) DEFECATION.—While to a certain extent a voluntary act, defecation is reflex to a degree. Indeed, it is highly probable that the inhibition of the act of emptying the rectum is the voluntary act, while the withdrawal of the inhibition (relaxing the sphincter ani) permits the act of defecation to be accomplished either entirely reflexly or by the aid of the voluntary action of the diaphragm and abdominal muscles.

It will be seen that these reflexes connected with the alimentary canal, may all be included under two forms of muscular activity: peristalsis and constriction. Strictly speaking, annular contraction of the alimentary tube, constriction, is a part of peristalsis, but as exemplified by the cardiac and pyloric ends of the stomach and by the sphincter ani muscles, constriction must be distinguished as a separate reflex act.

The subject of the reflexes connected with the alimentary canal would not be complete without mention of the occasional reverse movements.

(*g*) Emesis.—This is a reflex, very complicated in mechanism. In its simplest form it arises from irritant ingesta exciting spasmodic contraction of the stomach and extrusion of its contents through the relaxed œsophagus. But many other stimuli are capable of producing the motor phenomenon of vomiting. Thus nauseating odors, certain visual impressions, such as the sight of blood, or of objects which are associated in the memory with a former nausea are examples of the numerous sensory avenues through which the emetic reflex may be excited.

(*h*) Duodenal Regurgitation.—This may accompany the preceding or it may occur independently of it. Usually, however, it results in vomiting, as the presence of bile in the stomach is irritating, producing nausea.

II. *The Genito-Urinary Tract.*

(*a*) Micturition.—This act is allied to that of defecation, being voluntarily inhibited, and taking place reflexly on the withdrawal of the inhibition (relaxation of the vesical sphincter).

(*b*) Seminal Emission.—In the male, this may be a purely reflex act or it may be led up to by voluntary movements. In the latter case, illustrated by coitus, when the excitation of the glans penis has reached a certain stage the reflex contractions of the ejaculatory muscles proceed without possibility of further voluntary inhibition. In sleep the act may occur as a purely reflex one, the stimulus being supplied by too great warmth of the parts, irritation within the vesico-urethral canal or subconsciously by dreams.

In the female, excitation of the walls of the vagina, principally of the introitus and of its upper part, is the normal causal factor of this reflex act.

(*c*) Parturition.—The gravid uterus is capable of voiding its contents independently of voluntary control, as demonstrated in cases of transverse lesion of the cord above the parturition center. Usually in the second stage of labor, voluntary muscular contraction in the diaphragm and abdominal walls reinforces the reflex act.

III. *The Pupillary Reflex.*

When the light entering the eyeball is suddenly increased in intensity the iris contracts leaving a smaller pupil. Relaxation follows if the light is subdued.

When an object seen at a distance of two feet or more is quickly moved up near the eyes, and the gaze be fixed on it, the eyes converge and the pupils become narrow. This is the pupillary reflex of accommodation.

When the skin of the side of the neck is painfully irritated, the pupil expands in some individuals. These are the forms of the pupillary reflex, as it appears in health. In nervous disease there may be a dissociation of these forms, or there may be total immobility of the irides.

IV. *The Circulatory System.*

Throughout the system of blood vessels of the body we find an accompanying intricate nerve-supply, through which medium the muscular walls of the blood vessels are influenced to contract or to relax, and so control the volume of blood in a given part. In the heart, there are met everywhere in its muscular walls nerve-fibers originating in the cardiac ganglia, in those of the sympathetic system elsewhere, and in the medulla oblongata. None of these is subject to voluntary control, and stimuli arriving through them originate by irritation of the centers directly or by sensory impressions received by these centers. In the latter case it will be seen that a true reflex mechanism is called into play.

Dilatation and contraction of the smaller, peripheral blood vessels, giving rise to the phenomena of blushing and pallor respectively, are often due to sensory stimulation. This may result as a simple reflex act or with the interposition of an emotional (psychic) state. It may not be unjustifiable to consider the latter as a complex reflex action, as when the sight of an accident happening to another produces pallor, for example. It is also a well-recognized fact that an organ in active functional state is provided with more blood than when quiescent, *i. e.*, relaxation of its vessel-walls occurs in the presence of that which excites its function. As an example of this may be cited the stomach ; its blood vessels are comparatively turgid when food is taken, and contracted during a fast.

V. *The Respiratory Tract.*

Mention has already been made of the influence of the blood on the centers of respiration, varying with its degree of oxygenation. It is well known that respiration may not be voluntarily long suspended, the venous blood stimulating to renewed respiratory movements overcoming voluntary inhibition.

Certain volatile gases, as well as odors of certain kinds, stimulate respiration, while others depress it, both acting in a more or less complicated, reflex manner. Here too, an emotional state may be, as it were, interposed.

4. **Relation of Reflex Action to Higher Psychic Phenomena.**—From the foregoing will be seen in part the important rôle of reflex action. While the vegetative functions are nearly entirely maintained by it, in some form or other, many of the other body-functions are also purely reflex in their character. Nor is it difficult to conceive the complicated processes of perception, conception, memory, and other psychic phenomena, as reflex acts of greater complexity, *i. e.*, involving more sets of neurons than the simpler ones just considered.

c. The Location of Reflex Centers.

A diagram of the various reflex-centers corresponding to the reflex actions above mentioned, must of necessity include not only the axile motor cell-groups giving origin to the motor nerves that produce the respective movements, but also the various sensory centers in the same cerebro-spinal stem capable of stimulating those motor cell-groups. In the cases of the organic reflexes, as well as in those of many of the superficial reflexes, these sensory centers are very numerous and their connections with the motor centers multiplex. Furthermore, such a diagram could be of little service in diagnosis in the absence of other symptoms, since the loss of any given reflex is not evidence always of disease of either center, but may be due to a lesion located anywhere in the reflex-arc. As an aid, however, to the location of lesions, recognized as being in the cerebro-spinal stem, the following table may be of service :

Reflex.	Location of Center.
Plantar.	I and II. Sacral Segments.
Gluteal.	IV and V. Lumbar.
Cremasteric.	I–III. Lumbar.
Erectile of Penis.	I–II. Lumbar.
Abdominal.	VII–XI. Dorsal.
Epigastric.	IV–VII. Dorsal.
Mammary.	II–XII. Dorsal.
Scapular.	V. Cervical to I Dorsal.
Palmar.	VII. Cervical to I Dorsal.
Laryngeal.	X. Cranial Nerve. Bulb.
Pharyngeal.	IX. Cranial Nerve. Bulb.
Nasal.	V. Cranial Nerve. Bulb.
Conjunctival.	V. Cranial Nerve. Bulb.
Tendo-Achillis.	III–V. Sacral.
Ankle Clonus.	V. Lumbar.
Patellar.	II. Lumbar.
Extensors of Hand.	VI. Cervical.
Flexors of Hand.	VII–VIII. Cervical.

REFLEX.	LOCATION OF CENTER.
Pronotor of Hand.	VIII. Cervical.
Triceps.	VI. Cervical.
Supinator of Hand.	V. Cervical.
Biceps.	IV–V. Cervical.
Inf. Maxillary.	V. Cranial Nerve. Bulb.
Defecation.	IV. Lumbar.
Micturition.	III. Lumbar.
Seminal Emission.	IV. Lumbar to III Sacral.
Parturition.	I–II. Lumbar.
Intestinal Movements.	X. Cranial Nerve in Bulb.
Duodenal Regurgitation.	I–V. Dorsal (Splanchnic).
Pylorus.	X. Cranial Nerve in Bulb.
Gastric Movements.	X. Cranial Nerve in Bulb.
Emesis.	X. Cranial Nerve in Bulb.
Deglutition.	IX and X. Cranial Nerve in Bulb.
Sucking.	V, VII, and XII. Cranial Nerves in Bulb.
Respiration:	Tip of Calamus scriptorius.
Expiration.	X. Cranial Nerve in Bulb.
Inspiration.	X. Cranial Nerve in Bulb.
Circulation:	
Cardiac acceleration.	II–III. *et seq.*, Dorsal.
Cardiac inhibition.	X. Cranial Nerve in Bulb.
Vaso-motor dilatation, *blush.*	VII. Cranial to III Sacral.
Vaso-motor constriction, *pallor.*	II. Dorsal to II Lumbar inclusive.
Pupillary.	IV. Cervical to III Dorsal.
Vaso-motor.	Floor of the fourth ventricle.
Salivary secretion.	VII. Cranial Nerve in Bulb. Chorda Tympani.

3. THE TROPHIC FUNCTION OF THE SPINAL CORD.

In considering the functions of the spinal cord, sight must not be lost of the inherent property of cell-bodies here, as indeed everywhere throughout the nervous system, to maintain the nutrition of the more distant parts of the respective neurons. And as we have studied at length the functions of conduction and reflex action in the cord,—functions that are not performed by it exclusively,—so it will be proper here briefly to consider its trophic function.

Lesions of the cell-bodies themselves compromise the nutrition of the entire neurons; lesions of the branches alone affect the parts distal to the lesion. The degenerations resulting from such lesions have enabled us to trace with a fair degree of certainty the courses of the various neurons of the cord. (*Cf. Edinger* on the *Central Nervous System.*)

It is of prime importance to remember that the trophic influence of the motor neurons is extended beyond the motor end-plates to the muscles themselves; so that the nutrition of the muscles is intimately related to that of the nerve-trunks supplying them, both depending on the trophic influence of the cell-body. From this fact it follows that a destructive lesion of the cell-bodies of the peripheral motor neurons, as well as one interrupting their cellulifugal nerve-currents, causes not only degeneration in the respective nerve-fibers, but also atrophy of the muscles innervated by them. Non-destructive lesions may pervert the nutritional influence and produce a condition of dystrophy.

4. THE PHYSIOLOGY OF THE MEDULLA OBLONGATA OR MYELENCEPHALON.[1]

Like the spinal cord the medulla oblongata is both a path of communication between the higher centers and the periphery, and an independent center regulating functions of the utmost importance in the system.

a. The Medulla as a Medium of Conduction.

The paths in the medulla which transmit volitional motor impulses are the best understood; little is known regarding the functional activity of the numerous afferent and efferent tracts which connect the medulla with the cerebellum and cerebral ganglia, or of the specific functions of the various gray centers of the medulla itself. We are more indebted to the careful study which has been made of secondary degeneration of the medullary tracts and to the phenomena of disease than to any direct experimentation. Direct experiments on the medulla itself are full of difficulties and the results complicated.

That the pyramids are the paths of volitional motor impulse is proved most satisfactorily by the secondary degeneration which ensues in them in consequence of destruction of the cortical motor centers. The pyramid degenerates on the same side as the cortical lesion and as far as the point of decussation of the pyramids and thence the degeneration is continued downward in the pyramidal tract of the lateral column of the spinal cord on the opposite side and partly also, as will be remembered, in the anterior pyramidal tract of the same side, for a certain distance at least. Experimental evidence as to the result of section of the pyramids is somewhat uncertain, but in monkeys and man there can be no question as to their being the motor paths between the cortex and the anterior horns of the spinal cord.

As to the exact position and course of tracts serving cutaneous and general sensibility the same uncertainty, if not a greater, exists, as in respect to those paths in the spinal cord. But the best evidence, both physiological and pathological, goes to show that in the medulla oblongata they run on sides opposite to the parts where they are distributed. Above the decussation of the pyramids both motor and sensory tracts of the left half of the body lie in the right half of the medulla oblongata and *vice versa.*

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[1] Though the cord and medulla have been considered as a unit, it seems profitable to consider here briefly the functions peculiar to the latter.

b. The Medulla as an Independent Center.

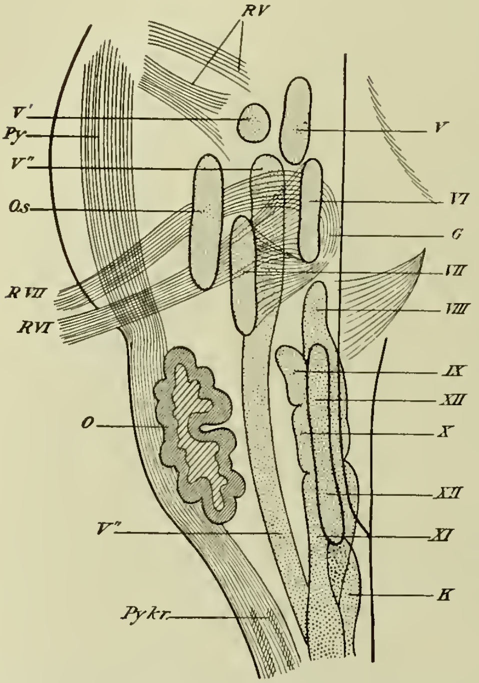
As such it presides over and regulates functions, on the due performance of which life essentially depends, as well as many others of considerable complexity but of less vital importance. All of the cranial nerves with the exception of the first four (viz., the olfactory, optic, motor-oculi and pathetic) have their primary origin in the medulla oblongata, and the third and fourth nerves, though springing from nuclei in the floor of the aqueduct of Sylvius, are also connected with the sixth pair through the posterior longitudinal tracts. Should all the encephalic centers above the medulla oblongata be removed, the mutilated organism, even of a warm-blooded animal, can live and breathe. The functions depending on the spinal centers will go on automatically and under reflex actions will be called forth in regions innervated, especially by the medulla itself. Thus the eyelids will close if the conjunctiva be touched ; the lingual, oral and facial muscles will contract and the ear twitch on irritation of the sensory nerves in reflex relation with the movements in question. But the movements capable of being elicited through the medulla oblongata are in many instances of a remarkable degree of complexity. Thus if a morsel of food be placed on the back of the tongue the combined and coördinated movements of the lips, tongue, palate and pharynx concerned in the mechanism of deglutition will be executed with as great precision as in perfectly normal conditions. In a young animal, so mutilated, the introduction of the nipple between the lips will be sufficient to set up the appropriate movements of sucking.

Occasionally human infants are born entirely without cerebral centers above the medulla oblongata, and yet an acephalous infant sucks and swallows as well as the perfectly developed child when put to the mother's breast. The medulla oblongata is the coördinating center of all these associated movements. Destruction of the medulla oblongata causes their instant and permanent annihilation.

The various afferent and efferent nerves concerned in the mechanism, viz., the hypoglossal, glosso-pharyngeal, facial and tri-facial, all spring directly from gray nuclei in the medulla. Fig. 287 shows the location of the principal centers of the medulla. The plexiform arrangement seen in the nerves which are concerned in the movements of the limbs is not manifest in the case of the cranial nerves, except in those of the pharyngeal plexus ; but there can be little doubt that there, as in the spinal centers, the nuclei of the various nerves concerned in special physiological coördinations are so connected together that a coördinate synergy is occasioned by stimulation just as readily as a single muscular contraction, on stimulation of an undivided muscle-nerve.

The movements concerned in the production of articulate speech have also probably their primary coördinating centers in the medulla oblongata. This is indicated more particularly by the phenomena of disease in this region in man. In "Bulbar Paralysis," the disease usually begins with slight defect in the speech and the patient has difficulty in pronouncing the dentals and linguals; the voice becomes nasal. The paralysis starts in the tongue and the superior laryngeal muscle gradually becomes atrophied and finally the mucous membrane is thrown into folds. When the lips become involved the patient can neither whistle nor pronounce the vowels "o" and "a." The muscles of the vocal cords waste and the voice becomes enfeebled. Death sometimes results from an aspiration pneumonia, sometimes from choking, more rarely from an involvement of the respiratory centers. The disease is found to depend on a process of degeneration specially in the nuclei of the hypoglossal, accessorius, vagus, facial and glosso-pharyngeal to a greater or less extent. The order of progression of the symptoms indicates a functional association of the nuclei which are implicated, but the exact anatomical details are still obscure.

FIG. 287.



Schematic transparent section of medulla oblongata, showing the principal centers. The numerals *V* to *XII* refer to the nuclei of origin of the respective cranial nerves. *V* is the motor nucleus; *RV*, the roots of the fifth nerve; *V'*, sensory nucleus; *V''*, sensory nucleus and ascending root; *RVI*, root of sixth nerve; *RVII*, root of seventh nerve; *Py.*, pyramid; *Pykr.*, decussation of the pyramids; *O.s.*, superior olive; *O*, olive; *G.f.*, genu of the facial. (STEWART.)

The medulla oblongata is a center of facial and of some other forms of what is usually regarded as emotional expression. Vulpian has shown that if a young rat be deprived of all encephalic centers above the medulla oblongata, pinching of the toes will cause not merely movements of the limbs but also a cry of pain. If the medulla be now destroyed pinching the toes will cause reflex movements of the limbs as before, but no cry will be elicited. The cry as of pain is, however, no real sign of pain, but only a reflex action of the laryngeal and expiratory muscles.

The coördination of the respiratory movements is one of the most important functions of the medulla oblongata. So long as the medulla is intact the function of respiration goes on in an automatic or reflex manner with the most perfect regularity and rhythm. When the medulla is destroyed respiration ceases and death ensues in all animals which cannot live by cutaneous respiration alone, like the frog. The chief center of coördination of the respiratory movements is situated near the beak of the calamus scriptorius, coinciding, or being in the closest relation, with the nuclei of the vagus nerves. From this point proceed the impulses which excite the associated and coördinated movements of the diaphragm, thoracic walls and air passages.

If the spinal cord be cut above the origin of the phrenic nerve the thoracic muscles and diaphragm speedily cease to act effectively for purposes of respiration, but as it has been shown, may still continue to act rhythmically and to respond to stimulation of certain sensory surfaces for a short period after section of the cord below the calamus. In some animals respiratory movements continue for a longer or shorter period after complete removal of the medulla oblongata. The respiratory center is in reality not a single cell group, but a bilateral group, each in relation to the vagus center of its own side. The two act normally in perfect unison, but they may be divided by a longitudinal incision in the median line, and then they lose their absolute synchronism and each half of the respiratory apparatus may perform its function independently of the other. The respiratory centers are in relation, however, not only with the afferent impressions conveyed by the vagus, but also with those of the sensory nerves in general and very manifestly with those of the head and chest. Hence a sudden stimulation of these surfaces, such as by a dash of water, causes active inspiratory movements. But a sudden stimulation of a sensory surface or sensory tract causes spasmodic arrest for a time, either in the state of inspiration or under certain circumstances of expiration. The rhythmical alternation of inspiratory movements is not, however, entirely dependent on reflex excitation, for respiratory movements may continue after all the afferent nerves connected with the center have been divided. In this case there is a true automatic activity influenced by the state of the blood itself. The diminution of oxygen and accumulation of oxidation products in the blood act as a stimulus to the respiratory centers. When the blood is artificially hyperoxygenated the movements of respiration come to complete standstill, a condition termed apnœa. Non-aëration of the blood, resulting from obstruction of the respiratory functions, powerfully excites the movements of both inspiration and expiration, and ultimately, if the obstruction continues, causes general convulsions of the whole body as in asphyxia. The respiratory mechanism, though essentially automatic or reflex, is to a great extent under the control of the will. It is by the volitional control we possess over the respiratory movements, that we are enabled to combine them with those of articulation for the purposes of speech and vocalization and in a similar manner by closure of the glottis and forcible contraction of the expiratory muscles we can aid the expulsion of the contents of rectum and genito-urinary organs. Our volitional control over the respiratory mechanism is limited.

Irritation of the branches of the vagus distributed to the alimentary canal induces vomiting, in which there is a combination of movements. The essentials are, dilatation of the cardiac orifice of the stomach and forcible pressure on this viscus by the expiratory muscles of the abdomen. It is customary to consider a special vomiting center, which is supposed to coördinate all these movements, but it is now held by physiologists that the facts do not justify a center distinct from the respiratory center, with such modifications as are conditioned by the starting point of the exciting stimulus.

The medulla oblongata also excites a controlling influence on the action of the heart and the state of the blood-pressure. The rhythmical movements of the heart are independent of the medulla oblongata and of the cerebro-spinal centers in general, and are conditioned mainly by the intrinsic ganglia of the heart itself; the heart muscle contracts rhythmically on stimulation apart from all nerves or ganglia.

It will be recalled that the inhibitory nerves of the heart run in the trunks of the vagi, also that cutting the vagi causes an increase in the number of heart-beats; stimulating the cut ends causes a diminution in the number of heart beats. A greater or less degree of inhibition is constantly maintained by the medulla, as is shown by the acceleration of the heart's action which follows section of the vagi. The fibers which cause the inhibition of the heart, spring from the spinal accessory nucleus and belong to the motor or centrifugal system. The accelerator nerves of the heart travel through the last cervical and first dorsal ganglia of the sympathetic. Stimulation of these nerves, as has been proved by Gaskell, increases the strength as well as the rate of the cardiac contractions.

The arterial walls are maintained in a continual state of tone which varies within certain limits, either automatically or in reflex relation with certain local and general afferent stimuli. The tone of the blood vessels is in a large measure dependent upon the gray matter of the spinal cord, the various segments of which may be regarded as more or less independent *vaso-motor centers.* But the predominating influence in the vascular system and the presiding influence over the variations in the blood-pressure depend upon the center in the medulla oblongata. As long as the medulla is intact, all the centers situated above it may be removed without greatly influencing the tone of the blood vessels or interfering with the variations of the blood-pressure. If, however, the cord be severed below the calamus scriptorius a general vaso-motor paralysis ensues with enormous fall of the blood-pressure, owing to the greatly increased vascular area. More precisely the center corresponds to the ganglionic cells of the upper oliva or the antero-lateral nucleus. This region, or its homologue in other animals, is termed the vaso-motor center and this center is supposed to be connected with all the afferent nerves capable of modifying its influence. Stimulation of the sensory nerves causes an excitation of the vaso-motor center and constriction of the arteries.

The medulla oblongata is a coördinating center of reflex actions essential to the maintenance of life. If all the centers above the medulla oblongata be removed life may nevertheless continue. The respiratory movements may go on with their accustomed regularity and rhythm; the heart will continue to beat and the circulation be regulated as under normal conditions; the animal may swallow food if it be placed in its mouth, may react in apparently purposive manner to impressions made on the sensory nerves, withdrawing its limbs or endeavoring to remove itself from the cause of irritation, or even utter a cry of pain, and yet will be merely an unconscious, unintelligent reflex mechanism.

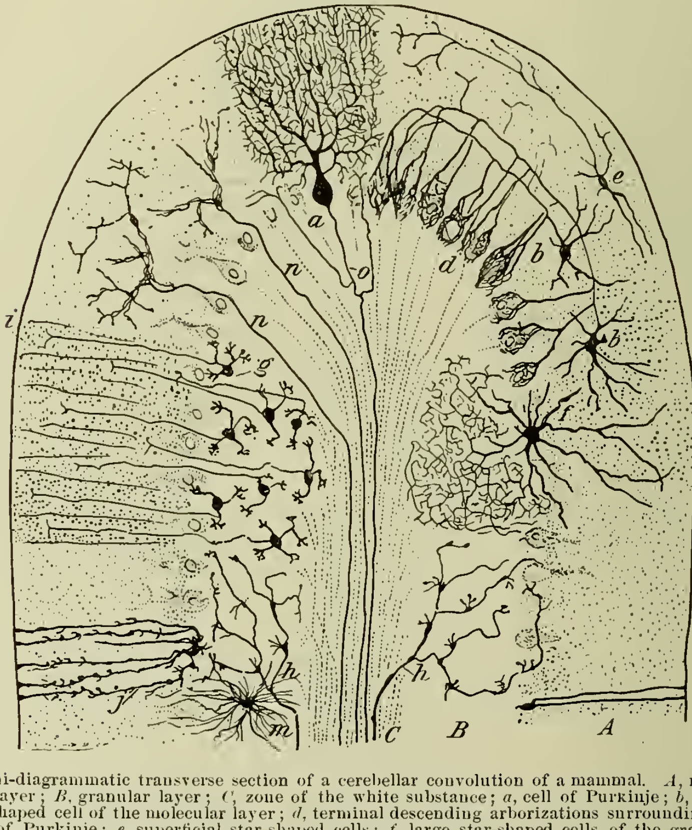
C. COÖRDINATION AND EQUILIBRATION.

THE PHYSIOLOGY OF THE CEREBELLUM OR METENCEPHALON.

1. COÖRDINATION: ADJUSTMENT OF MUSCULAR ACTION.

Regarded merely as a most complicated mechanism of bony frame-work and muscles, so adjusted as to permit almost an infinity of movements, changes of position, yet always in conformity with the natural force of gravity, even to the most casual investigator a correlating influence is apparent, an arrangement by which any change of position in a part of the body is accomplished through a nicely opposed action of two or more sets of muscles. Of these one relaxes as the other contracts, or where several groups are concerned different degrees of change in tension occur in the different groups, to just the extent necessary to produce the desired movement. Such a movement may be initiated by a distinct, voluntary impulse, but this voluntary impulse is apparently very simple in comparison with the complexity of the resultant muscular actions. Later, in considering the functions of the cerebral cortex, we shall see more clearly how such a result is obtained. But it is evident that however such actions are produced, there must be operative some controlling force, whereby the contraction and relaxation of opposed groups of muscles are properly adjusted, giving steadiness of action, and avoiding trembling, wavering, and other incoördinated movements. Such a force must be efferent, *i. e.*, exerted on the motor mechanism. And the center from which it rises must be in intimate relationship with those

Fig. 288.



Semi-diagrammatic transverse section of a cerebellar convolution of a mammal. *A*, molecular layer; *B*, granular layer; *C*, zone of the white substance; *a*, cell of Purkinje; *b*, small star-shaped cell of the molecular layer; *d*, terminal descending arborizations surrounding the cells of Purkinje; *e*, superficial star-shaped cells; *f*, large star-shaped cells of the granular layer; *g*, granules with their ascending axis-cylinders bifurcated at *i*; *h*, mossy fibers; *j*, neuroglia cell with plume; *m*, neuroglia cell of the granular layer; *n*, climbing fibers; *o*, ascending collaterals of the axis-cylinders of the Purkinje cells. (Cajal.)

afferent nerve-currents through which, either as general or as special sensation, we recognize our position relative to our surroundings. Such afferent impulses in all probability arrive through all the varied sense-apparatus, as may be learned when one or more is wanting.

This center of unconscious control of muscular movement determined by unperceived sensation, so to speak, is the cerebellum. The controlling force which it exercises is equilibration. Through its peduncles connecting its hemispheres with the cerebrum, with the medulla and cord, and with each other, it receives afferent impulses and emits efferent ones. (See Fig. 288.)

Though there is a more general agreement among physiologists as to the results of lesions of the cerebellum than of any other portion of the encephalon, there seems to be a correspondingly greater difficulty in finding such a definition of the functions of this organ as shall have a clinical and physiological value.

Experiments prove satisfactorily that destruction of the cerebellum in the lower mammals is followed by long continued, if not permanent, disorders of coördination and equilibration.

The cerebellum, like the cerebrum, does not respond to mechanical irritation. It has been found that if the induced current be applied to the cortex of the cerebellum in rabbits a series of ocular and other movements occur, depending upon the point which is stimulated. Electric stimulation of the cerebellum produces simultaneous movements of both eyes in different directions, according as the electrode is applied to different parts of its surface.

Besides these ocular movements, certain movements of the head and limbs were likewise produced. In some experiments in which the head was maintained in a fixed position, only movements of the eyes and also sometimes of the limbs could be observed, but when the head was released, the movements of the eyes coincided with movements of the head. Along with these effects the pupils were observed to become contracted on irritating the cerebellum. The contraction of the pupil is specially marked on the eye of the same side. The pupil may remain contracted for some time after the electric current has been removed. Vomiting or signs of sexual excitement have been observed.

Aside from these objective effects, there occur certain conditions of consciousness or subjective sensations which have an important bearing on the true significance of the cerebellar movements. These modifications of consciousness must, however, be regarded as coincident only and not connected with cerebellar action as such. The subjective phenomena depend not on the cerebellum, but on the cerebral hemispheres.

The cerebellum seems to be a complex arrangement of individual, differentiated centers which in associated action regulate the various muscular adjustments necessary to maintain equilibrium and steadiness of the body. We should therefore expect to find that a lesion which annihilates the functional activity of any of the individual cerebellar centers should manifest itself in a tendency to the overthrow of the balance in the direction naturally opposed by this center. This is in accordance with the facts of experiments. Stimulation of the anterior part of the middle lobe excites muscular combinations which would counteract a tendency to fall forward. Hence destruction of this part shows itself in a tendency to fall forward. In this we see both the negative effect caused by the removal of the one center, and the positive effects excited by the unopposed and antagonistic centers. In a like manner stimulation of the posterior part of the middle lobe calls into play the muscular adjustments necessary to counteract a backward displacement of the equilibrium; and a destruction of this region manifests itself in a tendency to fall backwards.

The lateral lobes of the cerebellum contain centers for complex adjustments against lateral, combined with diagonal and rotary, displacements to the opposite side, and hence, as has been found by experiments, lesions of the lateral lobes exhibit themselves in disturbances of the equilibrium either laterally to the side opposite the lesion or, as the resultant of lateral and rotary displacement, in rolling over to the side of the lesion. The effects of a lesion may therefore vary,—a fact which may account for some of the discrepancies among the results obtained by different experimenters.

Every form of active muscular exertion necessitates the simultaneous coöperation of an immense assemblage of muscular movements throughout the body to secure steadiness and maintain the general equilibrium; and on the hypothesis that the cerebellum is the center of these unconscious adjustments, we should expect the cerebellum to be developed in proportion to the variety and complexity of the motor activities of which the animal is capable. The facts of comparative anatomy and development are entirely in harmony with this hypothesis. In the reptiles and amphibia, whose movements are groveling and sluggish or of the simplest combination, the cerebellum is of the most rudimentary character, while in mammals it is richly laminated and the lateral lobes highly developed in proportion to the motor capabilities, represented in the motor zone of the cerebral hemispheres.

If we compare the relative development of the cerebellum in the several orders of the same class of animals we find it highest in those which have the most active and varied motor capacities, irrespective of the grade or organization otherwise; and the cerebellum of the adult is, relatively to the cerebrum, much more highly developed than that of the newborn infant, a relation which evidently coincides with the growth and development of the muscular system.

The mechanism of cerebellar coördination is essentially independent of consciousness and volition. The displacement of equilibrium in any direction not only calls into play by reflex or responsive action the compensatory motor adjustments, but also induces conscious or voluntary efforts of a similar or antagonistic, compensatory nature. Thus a tendency to fall forwards, while reflexly calling into action the muscular combinations which pull the body backward, may also excite consciousness and cause voluntary effort in the same direction. The same muscular adjustments which are capable of being effected by the cerebellum are also under the control of the will and may be carried out by the cerebral hemispheres independently of the cerebellum. Hence it is that lesions of the cerebellum do not cause paralysis of voluntary motion of the muscles which are concerned in these actions.

The statement has been made and adopted as a fact in certain quarters that lesions of the cerebellum produce paralysis of motion on the opposite side of body. In these cases, as has been pointed out by Vulpian, the hemiplegia is not the result of the cerebellar lesions as such, but of compression or interference with the subjacent tracts of the pons and medulla. As these decussate in the medulla oblongata the effects of compression by a tumor of the lateral lobe of the cerebellum is paralysis of the opposite side of the body. Lesions of the cerebellum which do not exert such an influence on the subjacent tracts do not cause hemiplegia on the opposite side.

The disturbance of equilibrium is always most marked immediately after the infliction of injury to the cerebellum. This, which has been by many looked upon as a sign of irritation, is to be accounted for by the sudden derangement of the self-adjusting mechanism on which the maintenance of equilibrium mainly depends. As, however, the animal may supplement the loss of this mechanism by conscious efforts, in process of time it acquires the power of voluntary adaptation and thus is enabled to maintain its equilibrium, though perhaps with less degree of security than before.

The more extensive the lesions the greater the disturbance of the mechanism and the greater the difficulty of effecting through conscious effort all the muscular adjustments necessary to maintain the balance. The disturbances of equilibrium are therefore of a more enduring character and it is only by a long process of training that volitional accommodation replaces a mechanism essentially independent of consciousness. Even should this point be reached, the constant attention necessary to preserve steadiness of movement and prevent displacement of equilibrium would be a heavy strain on the animal's power; and it would be in accordance with this condition that prolonged or varied muscular exertion should cause great apparent exhaustion, actually verified by experiments on animals.

The cerebellum was regarded by many of the older writers as the seat of common sensibility. The opinion was founded chiefly on the continuity of the posterior columns of the spinal cord with the restiform bodies. That these are mediately related with the posterior columns through the olivary bodies, has been established by the researches of Meynert and other anatomists, the relation being mainly crossed, *i. e.*, the restiform body on one side being related to the opposite posterior column. The posterior columns being regarded as the path of common or tactile sensation, the axiom that the cerebellum was a seat of common sensibility seemed well founded. But more recent investigations into the sensory paths of the spinal cord do not support this view of the functions of the posterior columns. Brown-Sequard has shown by direct experiment that section of the restiform bodies does not cause loss of tactile sensation. These facts in conjunction with the results of experimental lesions and diseases of the cerebellum afford overwhelming evidence against the view that the cerebellum is the seat of common sensation. Neither Flourens, Vulpian, Lucieni, Ferrier nor other recent experimenters have ever observed cutaneous anæsthesia in animals deprived of the cerebellum.

Through what system of fibers, or pathway, does the cerebellum act so as to call forth the muscular adjustments requisite for equilibration? If the restiform bodies be examined for the purpose of ascertaining this point one finds that if this tract be injured the most turbulent disorders follow, similar to injury of the semicircular canals. If the olivary bodies be injured disturbances of the equilibrium result, with rolling, forced movements and deviation of the optic axes similar to those caused by lesions of the middle cerebellar peduncles. These facts render it probable that it is through the medium of the olivary bodies that the impressions conveyed by the posterior columns of the cord ascend to the cerebellum through the restiform tracts, and that it is the interruption of these connections which leads to disorders of the equilibrium. The restiform bodies are also related, as has already been described, to the direct cerebellar tracts derived from the cells of Clarke's column. It seems fairly well established that the restiform tracts convey tactile impressions which excite and regulate cerebellar coördination.

Relations to the Labyrinth.

The relation between the cerebellum and the auditory nerve is suggested by anatomical considerations. The so-called auditory nerve ought to be subdivided into the vestibular nerve or nerve of tonus, coördination, and equilibration, and the cochlear nerve or nerve of hearing, just as in times past the seventh nerve of Willis became generally known as the facial nerve and the auditory nerve. The vestibular nerve passes from the ampullæ of the semicircular canals partly to the dorsal auditory nucleus, and partly to the cerebellum, perhaps directly, by way of the direct sensory cerebellar tract in the inner division of the corpus restiforme. This dorsal auditory nucleus is further connected on the one hand with the superior olive having connections with the posterior quadrigeminal bodies, and on the other hand with the cerebellum. Further than this almost nothing is known of the central path of the nerve. The cochlear division of the auditory nerve seems to have nothing to do with the cerebellum physiologically, because lesions of the cerebellum do not impair the sense of hearing in animals, nor do diseases of the cerebellum in man cause deafness, except in such cases as lead to direct implication by means of pressure or otherwise of the cochlear division of the auditory nerve or the ventral auditory nucleus.

There is thus an important influence exerted by the semicircular canals upon the function of coördination, and we have just noted the anatomical foundation for this influence in the connections which exist between the labyrinth and the cerebellum. There is further a remarkable and significant similarity between lesions of the individual semicircular canals and injury of certain regions of the cerebellum, and also between direct irritation of the canals and electrical irritation of different portions of the cerebellar cortex. Experiments involving the local irritation of the labyrinth in man have led to an hypothesis which assumes that stimulation of the superior vertical canal causes phenomena similar to those produced by irritation of the posterior cerebellar centers; stimulation of the posterior vertical canal, phenomena similar to those produced by irritation of the anterior cerebellar centers; and stimulation of the horizontal canal, phenomena similar to those produced by irritation of the lateral cerebellar centers.

Various forms of irritation applied to the semicircular canals also bring out ocular movements and movements of the head and body exactly like those produced by stimulation of various portions of the cerebellum. Similarly, if air or liquids be injected into the ear of man where the membrana tympani has been ruptured, the eyes turn to right or left, depending upon the side which is injected, and a feeling of vertigo occurs.

Animals deprived of their cerebral hemispheres are not only able to maintain their equilibrium but are also capable of coördinated locomotion in their usual manner. The mechanism of this locomotion, like the mechanism of equilibration, consists (1) of an afferent system and (2) of a coördinating center, (3) an efferent or motor system by which the center is brought into relation with the muscles of the trunk and limb.

Locomotion involves a vast complexity of motor adjustments of the head, trunk and limbs, beyond the simple combinations of the muscles of the limbs which are coördinated in the spinal cord. The center of gravity is continually varying with each movement of the limbs; this necessitates perpetual readjustment of the trunk and limbs. By stimulation of the spinal cord below the calamus scriptorius the limbs of rabbits, as shown by Ludwig, may be thrown into coördinated and alternating actions, such as running and leaping, but the spinal centers alone are unable to provide for the execution of these movements. These require the presence and activity of the mesencephalic and cerebellar centers. When one learns to execute movements, the sense of vision aids in a large measure in directing the body and limbs to carry out the end desired, and one is guided also by the sensations and impressions arising in connection with muscular action. When these movements have been learned neither vision nor the sense of muscular action seems necessary and the most complex coördinations can be executed with precision without attention or consciousness. What has at one time required a conscious effort becomes an organized reflex, provided for in the mechanism of the lower centers.

Instinctive or Emotional Expression.

Animals deprived of their cerebral hemispheres are still capable of exhibiting, in response to various forms of sensory stimulation, special and general reactions, more or less complex, which do not at all differ in character from those which are associated with emotion or feeling.

The outward expression of feeling does not necessarily imply the existence of pain or feeling as a state of consciousness. As all the physical manifestations of feeling are capable of being called forth in animals deprived of their cerebral hemispheres, which alone are the substrata of consciousness, we must regard them as merely the reflex or instinctive response of centers in which sensory impressions excite variously the motor, vaso-motor, and secretory apparatus. The phenomena observed in animals deprived of their cerebral hemispheres are in all respects analogous to those observed in human beings under the influence of chloroform which, as proved by actual experiment, first annihilates the excitability of the hemispheres, a condition coinciding with abolition of consciousness,—but the mesencephalic and lower centers retain their excitability long after this point has been reached. Hence with impressions which under normal conditions would excite not only pain but also accompanying groans, cries, or other physical manifestations, when the cerebral hemispheres have been removed the physical manifestations alone occur, and conscious suffering is absent.

The centers of emotional expressions are therefore situated below the centers of conscious activity and ideation, and must necessarily be in relation with every form of centripetal and centrifugal impulse through which signs of feeling may be induced or manifested. These conditions are not furnished below the mesencephalic centers. With these, however, as the experiments of Vulpian and others have shown, every form of reaction, excepting perhaps the reactions special to the olfactory nerve, may be elicited in response to appropriate peripheral stimulation, in all respects like those shown by unmutilated animals.

But, although the facts above related prove that in the absence of the cerebral hemispheres, acts of extraordinary complexity,—equilibration, coördinated locomotion, adaptive reactions and signs of feeling in response to sensory stimulation,—are capable of being carried out, it is a problem of surpassing difficulty to analyze the mechanism of the various manifestations and specialize the centers in which they are individually localized.

2. EQUILIBRATION: THE MAINTENANCE OF EQUILIBRIUM.

An animal deprived of its cerebral hemispheres is capable, not only of maintaining its equilibrium, if undisturbed, but of regaining it when overthrown. Considerable complexity and diversity of muscular movements all adapted for the purpose, are called into play according to the conditions under which the animal may be placed.

The maintenance of equilibrium involves the conjoint operation of three separate factors: (1) A system of afferent nerves and organs. (2) A coördinating center. (3) Efferent tracts in connection with the muscular apparatus concerned in the action. The faculty of equilibration is overthrown by lesions of the afferent apparatus alone or by lesions of encephalic center alone, or by lesions of the efferent tract alone or by conjoint lesions of all. Various degrees and forms of disturbance of this function will result, according to the nature, extent and position of the lesion. In many respects the maintenance of the equilibrium resembles the tone of the muscles. Lesions of the afferent nerves, central ganglia or motor nerves destroy the tone of muscles, and according as this occurs in both or only in one group of antagonistic muscles we have complete muscular flaccidity, flexion, or lateral distortion. So in regard to equilibrium, similar lesions may cause complete overthrow, or various forms of distortion exhibited as reeling, staggering, rotation, etc.

The *afferent apparatus* is of a compound nature but mainly consists of three great systems, upon which the maintenance of equilibrium and coördination depends. These three systems are: (1) Organs for the reception and transmission of common sensory impressions. (2) Organs for the reception and transmission of visual impressions. (3) The semi-circular canals of the internal ear and their afferent nerves. Each of these systems will be considered separately.

1. **The Influence of Tactile Impressions.**—A frog deprived of its cerebral hemispheres, but in which the optic lobes and cerebellum are intact still preserves the power of maintaining its equilibrium. If now the skin be removed from the hinder extremities the animal at once loses this power and falls like a log, when the basis of support is tilted. The removal of the skin has destroyed the receptive organs of those sensory impressions which are necessary to excite the coördinating center so that the various combinations of muscles shall maintain the animal in equilibrium. It is a law laid down by Volkmann and verified by all subsequent observers, that reflex reactions are more capable of being excited by impressions on the peripheral extremities of afferent nerves than by stimuli applied to any other part of their course. A similar result ensues in man, as has been shown by Heyd when the soles of the feet are rendered insensible by chloroform or refrigeration. The individual experiences great difficulty in maintaining equilibrium when the eyes are shut, and he oscillates and sways in a very pronounced manner. In locomotor ataxia, one of the characteristic symptoms in addition to the locomotor incoördination, is the difficulty, or absolute impossibility, of maintaining the equilibrium when the eyes are shut. When the individual tries to stand with his feet together and his eyes shut, he oscillates greatly or actually falls if unsupported, and it is difficult or altogether impossible for him to stand or walk in the dark though the eyes are open. In this disease there is diminution or absence of sensibility to tactile impressions, so that the patient feels as if something soft were interposed between his feet and the ground, or he does not feel the ground at all. The impairment or abolition of tactile sensibility is capable of being compensated for, up to a certain point, at least, by visual and other forces, but when the eyes are shut, or the light withdrawn, equilibrium becomes difficult or impossible. Even in normal individuals the visual sense aids the tactile power. If a perfectly normal person stands with his feet close together and the eyes closed he perceives more or less oscillation. Consciousness is not a necessary condition for perfect equilibrium. If, however, equilibration be deranged the condition is made known to the consciousness in a painful manner in the form of vertigo or sense of insecurity.

2. **The Influence of Visual Impressions.**—Equilibration and motor coördination may be acquired in the first instance and exercised without the aid of the eyes, as exemplified in those born blind. But in general, the motor adjustments used in regulating equilibrium are guided by the sense of sight. The child who learns to walk keeps his eyes continually on his limbs and the surrounding objects, and sees that his movements are made in accordance with the end desired.

When the movements become organized and automatic by frequent repetition the guidance of the eyes ceases to be so necessary and the impressions, conditioned by the movements themselves, are sufficient to insure the requisite simultaneous and successive motor adjustments. But, even then, visual impressions, though not closely affecting consciousness, are not inoperative, as is proved by the uncertain and wavering character of motor adjustments, even of the most habitual or automatic character, when the eyes are shut or the light withdrawn. When there is defect or total default of tactile sensibility, equilibration is impossible, except with the aid of vision. The sense of sight may compensate for a total absence of tactile (including muscular) sensibility, and an individual who has no sensibility in his lower extremities, and who falls like a log when he shuts his eyes, may stand or walk if he looks at his feet. This, however, always implies strained effort and speedily induces fatigue.

It would seem that the act of keeping the eyes open is of itself an aid to equilibration, though the eyes are useless as organs of vision. It has been observed that patients suffering from locomotor ataxia who were previously entirely blind, and able to stand with their eyes open, oscillate much more when they are shut. This is probably due to the interruption of the act of fixed attention, of which the steady gaze, even with sightless orbs, is the physical expression.

The influence of vision on equilibration is further shown in the disturbances created by unusual movements in the field of vision, either by movements of the objects themselves, or induced by faults in the oculo-motor apparatus. We associate position in space, not only with certain tactile sensations, but with a certain definite relation to surrounding objects. When the whole field of vision is in motion, or the positions of familiar objects are distorted by obliquity of the optic axis, there is a disturbance of the customary relations between the visual and tactile sensations and a distressing sense of insecurity results—the individual not being able to discriminate clearly whether he himself or the objects around him are in motion or displaced. The difficulty of equilibration under such circumstances gives rise to the sense of vertigo, which is merely the subjective side of the physiological disturbance. Oscillation of the eyeballs or nystagmus, or the occurrence of paralysis in one of the ocular muscles, such as the external rectus, is a familiar cause of the vertigo which is caused by a lack of harmony between the visual and tactile experiences and associations of our relations to surrounding objects. It has been found by Cyon that pigeons are similarly affected by distortion of the optic axis. On placing prisms before their eyes he observed marked disorder of equilibrium amounting, in some cases, to actual falling down.

3. **The Influence of Labyrinthine Impressions.**—The impressions which are generated in the semicircular canals of the internal ear form the most important factor in the afferent apparatus of the mechanism of equilibration and more clearly indicate the essentially reflex nature of the mechanism.

When the membranous canals are injured very remarkable disturbances of equilibrium ensue which vary as Flourens first pointed out with the seat of lesion. According to the observations of Flourens and Cyon on pigeons, when the horizontal canal is divided on the side, the head is thrown into a series of oscillations in a horizontal plane around the vertical axis. When the posterior vertical canals are divided the disturbance of equilibration is of a similar character, but more violent. In this case the movements of the head are in a vertical plane around a horizontal axis. Section of the posterior vertical canals causes movements of the head from behind forward and from right to left, or *vice versa*. There is profound disturbance of equilibration and the animal tends continually to turn somersaults heels over head. The plane of the movements of the head in this case is diagonally around a horizontal axis. Thus, analysis of the movements consequent on section of the respective canals, shows that they take place in the plane of the canals operated on.

It has been observed that the disturbances of equilibrium after section of one or more of the canals on one or both sides are of comparatively short duration. When the whole of the semicircular canals on one side are destroyed the disturbances of equilibrium are also transitory. When all the canals are destroyed on both sides the disturbances of equilibration are of the most pronounced character. Goltz describes a pigeon so treated, which always kept its head with the occiput touching the breast, the vertex directed downwards with the right eye looking to the left, and the left looking to the right, the head being almost incessantly swung in this position in a pendulum-like manner. Cyon says it is impossible to give an idea of the perpetual movements to which the animal is subject. It can neither stand, nor lie still, nor fly, nor maintain any fixed attitude. It executes violent somersaults, now forward, now backward, rolls round and round, or springs in the air and falls back to recommence anew. It is necessary to envelop the animals in some soft covering to prevent their dashing themselves to pieces by the violence of their movements, and even this is not always successful. The extreme agitation is manifest only during the first few days following the operation, and the animal may then be set free without danger, but is still unable to stand or walk, and tumultuous movements come on from the slightest disturbances.

In what manner do injuries of the semicircular canals cause disorders of the equilibration? The first supposition which suggests itself is that these disorders are related to the disturbance of the sense of hearing. It has, however, been abundantly proven that this is not the case.

The phenomena observed in connection with lesion of the semicircular canals clearly point to these organs as the source of impression which are necessary for the maintenance of the equilibrium and without which optic and tactile impressions alone barely suffice even after prolonged education.

4. **Symptoms of Cerebellar Disease.**—The most characteristic symptom of cerebellar disease in man, apart from indirect complications, is an uncertain or reeling gait, like that of alcoholic intoxication. But this symptom, though general and pathognomonic, has not always been observed in cases in which it has been proved by post-mortem examination that disease of considerable extent has existed in the cerebellum during life. Unless the disease has been of a sudden character, none of the violent and tumultuous disorders which characterize the abrupt lesions of physiological experiments have been met with, and this is a fact which the gradual subsidence of the symptoms in the lower animals would lead us to expect. It is also true that limited lesions can run their course without manifest symptoms, particularly when the lesion involves a lobe or part of it. But when the whole cerebellum has been involved, or has been greatly or completely atrophied, careful observation has never failed to discover a greater or less degree of awkwardness of movements and instability of equilibrium.

Many of the cases of atrophy of the cerebellum on record have been found in imbeciles, but it is clear from other evidences that the imbecility or impaired intelligence is only a symptom of cerebral defect coincident with that which has led to the cerebellar symptom. The most remarkable case is that of Alexandrine Labrosse, reported by Corbette. This girl lived to the age of eleven years, and it was found after death that the cerebellum was entirely atrophied, its place being occupied by a cyst containing serum. Physically she was well developed for her age, but she was five years of age before she was able to stand, and at the age of seven she was very insecure on her legs and often fell. Her intelligence was defective and her articulation indistinct, but all her sensory faculties were normal.

An almost equally remarkable brain was examined by Ferrier. It was that of a girl who died of phthisis at the age of fifteen. Nothing was ascertained respecting her early life. She was somewhat weak in intellect, but not to any great extent, and had the narrow palate of the imbecile. Owing to this her articulation was somewhat indistinct. No deficiency existed as regards her sensory faculties, general or special, and the only peculiarity observable in her motor powers was a general muscular weakness and a tremor of the hands when she was using them, but this was attributed to the debility associated with her phthisical condition, and she could walk well and steadily, though she was never known to run.

After death no abnormality could be detected in the cerebrum, which was well developed, but the cerebellum was very illy developed; in fact, it was arrested at a very early stage. The left lobe was a mere papilla, the vermiform process a minute nodule, obscurely marked with laminæ, while the right lobe, which contributed the main portion, was only a half of a square inch in superficial area and only a quarter of an inch in thickness at its base. The pons was indicated by only a few transverse fibers, which barely concealed the pyramidal tracts in their course from the foot of the cerebral peduncles. The corpora quadrigemina had a normal size and appearance; the olivary bodies of the medulla oblongata were only obscurely indicated. With the exception of the cerebellum and the peduncles, which were reduced to insignificant dimensions, the rest of the brain and all the cranial nerves were perfectly normal in appearance.

It is evident from examination of repeated cases that, though cerebellar disease in man is frequently associated with symptoms similar to those which result from experimental lesions in the lower animals, yet the organ may be almost entirely degenerated without any more obvious symptoms than a greater or less degree of unsteadiness of movement or instability of equilibrium. If the cerebellum were absolutely necessary for the coördination of movements it would be impossible to harmonize the actual facts of clinical observations with a hypothesis so formulated. For, in the case of Alexandrine Labrosse, it would have been impossible for her to walk at all if the coördinated movements were dependent on the cerebellum as *the* organ of equilibration. If, however, we regard the cerebellum as *an* organ of equilibration, it will be possible to bring all the symptoms, acute and chronic, into harmony with this hypothesis.

D. VISION, COÖRDINATION OF EQUILIBRATION MOVEMENTS.

THE PHYSIOLOGY OF THE CORPORA QUADRIGEMINA[1] OR MESENCEPHALON.

The fibrous connections of the two anterior quadrigemina are as follows:

(I) With the cortex of the occipital lobe of the same side through anterior arms of the corpora quadrigemina. (II) With the posterior and lateral tracts of the spinal cord. (III) With the optic tract, through the anterior arms of the corpora quadrigemina.

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[1] Of the mesencephalon the corpora quadrigemina represent only the roof. The optic tracts form a prominent feature of the walls of the mid-brain. The base of the mid-brain includes prominent "masses of fibers which arise in the fore-brain and inter-brain and traverse the mid-brain on their way to parts beyond" (Edinger). It is from nuclei in the base of the mid-brain that the oculo-motorius and trochlearis arise.

The fibrous connections with the posterior quadrigemina are the following: (I) With the cortex of the temporal lobe of the same side through the posterior arms of the corpora quadrigemina. (II) With the tegmentum through the lemniscus lateralis, which delivers to the posterior corpora quadrigemina acoustic fibers, probably also fibers from the posterior tract of the spinal cord. (III) With the inferior commissure of the optic tract through the posterior arms of the corpora quadrigemina.

The optic lobes or corpora bigemina of fishes, batrachians and birds are structurally homologous with the anterior corpora quadrigemina of mammals.

FIG. 289.

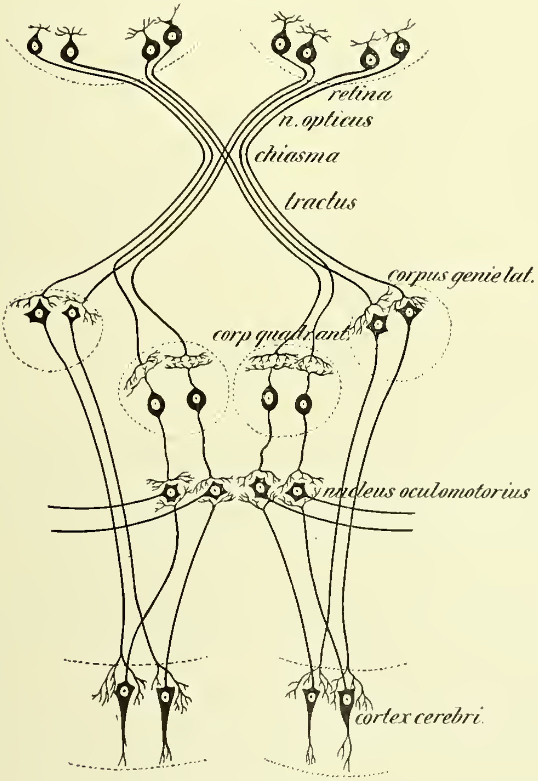
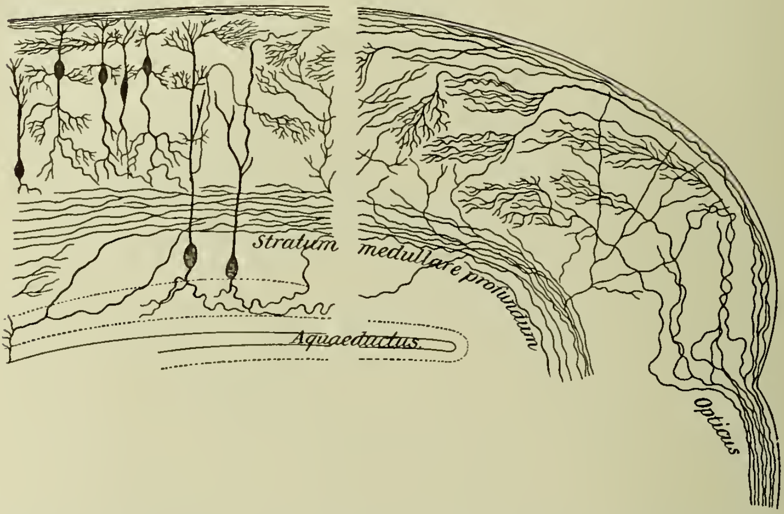


Diagram of the probable relations of some of the nerve-cells and fibers belonging to the retinal and central visual apparatus. (SCHAEFER.)

The obvious anatomical connection between the optic tracts and the anterior quadrigeminal tubercles of mammals is sufficient to indicate that these centers have some important relations to retinal impressions. (Study Fig. 289.)

The facts of anatomy as well as those of physiological and pathological experiments indicate that the corpora quadrigemina, though not the centers of vision proper, are centers of coördination between retinal impressions and motor reactions or adjustments of considerable complexity. It is difficult, if at all possible, to differentiate clearly between the effects of lesions of the corpora quadrigemina and of those tracts with which they are related. In this connection a study of Fig. 290 may be suggestive.

Fig. 290.



Showing the minute structure of the mid-brain-roof. Two sections are placed side by side for comparison of the layers. The right-hand section is from a frog; the left-hand one from a lizard. Various connections may be traced between the optic tract and the stratum medullare profundum. When one remembers that the *tr. tecto-spinales et tecto-bulbares* are traced into the stratum medullare profundum we see a basis for Edinger's suggestion that "through this structure there arises an extraordinarily great opportunity for the transmission of light impressions to the general sensory tract." (Edinger, V. edit., p. 116.)

When the hemispheres are removed the pupils will contract to light and the eyes are moved in response to retinal impressions and in accordance with variations in the position of head and body.

The movements of the iris and eye-muscles are presided over by the nuclei of the third and fourth nerves situated in the ventral aspect of the aqueduct of Sylvius. After removal of the cerebral hemispheres in dogs, it has been found that the application of electrical stimulation to the floor of the aqueduct of Sylvius and posterior part of the third ventricle gives rise to different ocular movements, according to the position of the electrodes.

Flourens found that destruction of the optic lobes in birds caused blindness and dilatation of the pupils with cessation of their reactions to light; and he also found that the relations of the optic lobes were entirely crossed, *e. g.*, destruction of the left lobe causing total loss of vision in the right eye and destruction of the right lobe causing total loss of vision in the left eye. The cross relations between the eyes and optic lobes have their foundation in the decussation of the optic tracts in the optic chiasma, but the extent of the decussation varies in different animals. Destructive lesions of one optic tract in man causes homonomous hemianopsia of both eyes. Experiments have shown that after enucleation of one eye in cats and dogs, partial atrophy occurs in both optic tracts, but to a much greater extent in the tract of the opposite side.

It has been observed that lesions of the corpora quadrigemina in various animals give rise to marked disturbances of equilibrium and irregularity of movement. While able to make coördinated movements of defense and the like, they had entirely lost the power smoothly to coördinate equilibration movements. That this cöordination of equilibrium is not due merely to the blindness resulting from the destruction of the optic lobes is shown by the fact that a frog deprived of its cerebral hemispheres and also of its eyes, is still able to maintain its equilibrium as before. If the optic lobes alone are destroyed, exact equilibration is impossible, even though all the other encephalic centers are retained.

Effects of Irritation.—The excitability and effects of irritation of the corpora quadrigemina or optic lobes, by various stimuli, have been differently stated by different observers. Ferrier maintains that mechanical irritation of the surface of these bodies is capable of inducing distinct indication of excitability. The act of merely touching these ganglia with a sponge is sufficient to cause general and more or less indefinite movements of the trunk and limbs. The slightest superficial puncture of the corpora quadrigemina in rabbits causes them to start suddenly and bound away as if in great agitation and alarm. These symptoms speedily subside and it is almost impossible to discover any signs of anatomical lesion from the slight puncture which is sufficient to give rise to these manifestations. Much, however, depends on the vital condition of these ganglia at the time of experiment. When they are exhausted by shock or hemorrhage or paralyzed by narcotics excitation may have little or no perceptible effects. The optic lobes have been found extremely sensitive to electrical currents.

The explanation of the effects of irritation of the corpora quadrigemina and of the relation between these and the effects of destructive lesions, is a matter of speculation only. Though electrical stimulation is not strictly localizable, and there is always a risk of diffusion, it has been shown that mere mechanical irritation of the surface of the corpora quadrigemina is sufficient to produce motor manifestations, in which case obviously conduction to subjacent or neighboring tracts can play no part. The strength of current sufficient to produce active manifestations when applied to the surface of the corpora quadrigemina is very weak and barely perceptible when applied to the tip of the tongue; so that the risk of diffusion is very slight, and it is a fact which cannot be explained away by mere diffusion to subjacent structures. Irritation of the posterior tubercles differs from that of the anterior in at least one important particular, viz.: the excitation of cries of various kinds. These are not observed on irritation of the anterior tubercles. If it were merely a matter of diffusion to subjacent tracts, the same results should occur in both cases. Then again there is an anatomical difference between the anterior and posterior quadrigemina which supports the view that the phenomena are due to the direct excitation of these ganglia as such. The surface of the anterior quadrigeminal bodies is composed of zonal fibers, superficial gray matter and medullary fibers which are directly related to the optic tracts, structures, however, are not found in the posterior bodies.

Human pathological and clinical observation teaches that the constant symptoms accompanying disease of the corpora quadrigemina are: stumbling gait, disorders of vision, and sometimes disturbances of hearing.

E. THE PHYSIOLOGY OF THE INTER-BRAIN OR THALAMENCEPHALON.

Almost nothing is known of the physiology of the inter-brain. Certain features of its structure are suggestive, however, of functions which it may some time be demonstrated to possess.

(*a*) As a Relay Station the inter-brain seems to serve its principal function. "The nuclei of the inter-brain receive fibers from the basal ganglia of the fore-brain and give off posteriorly new tracts to centers which lie at a lower level. * * * We see in the thalamencephalon a great center which is inserted between an important part of the cerebrum and nearly all other parts of the brain" (Edinger, V. Edit., p. 134). That the development of this segment of the brain is largely dependent upon that of the cerebrum is evident from the fact that "*with the development of an extended cerebral cortex more and more bundles appear which pass from it into the ganglia of the thalamus*" (Edinger, p. 135).

(*b*) As a Sensory Center the inter-brain must be given some credit. Fig. 289 shows the lateral geniculate body, a part of the thalamus, as a way station between the retina and the cerebral cortex of the visual center in the occipital lobe. In a similar way the internal geniculate body is a way station on the path of auditory sensation.

F. THE PHYSIOLOGY OF THE CEREBRUM OR PROSENCEPHALON.

1. INTRODUCTORY.

a. The Vascular Supply of the Brain.

1. **The Arteries of the Brain.**—Our knowledge of the vascular supply of the brain has been rendered more accurate owing to the independent labors of Huebner and Duret. The entire arterial supply of the brain has been divided into two systems, viz: a basal and a cortical arterial system. Here we shall have to deal more particularly with the latter. For the full description of the source and arrangement of the basal system the student is referred to his anatomical text-books.

(*a*) THE DISTRIBUTION OF THE CEREBRAL ARTERIES.—From the basal arterial system as represented by the circle of Willis, numerous small branches pass off nearly at right angles and enter the ganglia near the base of the brain; these are called terminal or end-arteries because they do not anastomose with one another nor do they anastomose with the vessels of the cortical arterial system. The anterior cerebral and the middle cerebral are the main arteries of the fore-brain. The former supplies the superior frontal and anterior two-thirds of the middle frontal convolution and the upper extremity of the ascending frontal. Its branches are distributed to the upper half of the median surface of the cerebral hemisphere from the frontal apex to the sulcus occipitalis, and on the lateral surface to the superior half of the frontal and parietal lobes.

The middle cerebral artery supplies the lower half of the frontal and parietal lobes, and the upper two-thirds of the temporal and occipital lobes on the lateral surface of the hemisphere, while on the median surface it supplies a small area, including the hippocampal region and the apex of the temporal lobe. It supplies the corpus striatum and the caudate and lenticular nuclei.

The posterior cerebral artery is distributed to the posterior two-thirds of the basal aspect of the brain, extending up laterally to include the lower third of the temporal and occipital lobes, and on the median surface, the inferior one-fourth.

From the distribution of the anterior, middle and posterior cerebral arteries we see that they determine the blood supply to certain regions. Each main artery gives off secondary and tertiary branches. These tertiary branches in their turn give off numerous fine arterioles, which, according to Duret, do not anastomose with one another, although a communication may take place to a certain extent between the branches of contiguous areas. Opinions differ considerably upon the question of anastomosis between the vessels of the cortical system. Huebner, basing his opinion upon the result of his injections, believes that there is a free anastomosis between the main vessels, and also between the secondary branches of the vessels of the cortex, the anastomosis being effected through vessels not less than a millimeter in diameter. He does not believe that collateral compensation is effected solely through the circle of Willis. In consequence of this view, objection is taken to the statement that an artery supplies any definite region or convolution. In support of Huebner's view, we have the fact admitted by Charcot that in certain cases of arterial obstruction by embolism or thrombosis there is an exemption from softening which would point to the establishment of a collateral circulation. Duret contends that such an anastomosis is absent or extremely rare, and he maintains that it is only through the terminal filaments of the branchlets that communications occur. Such communications, however, he believes may vary in number in different individuals. Cohnheim also maintains that there are anastomoses between the larger branches of trunk arteries, but that all the cerebral arteries more or less resemble true terminal or end arteries, in that they communicate with other vessels through their ultimate capillary loops only.

(*b*) Structure of the Cerebral Arteries.—The cerebral arteries have less muscular element than those of the body generally. In the larger arteries the tunica adventitia is directly continuous with pia mater, whilst in smaller vessels the sheath becomes an extremely fine membranous investment, either structureless or faintly striated, and with nucleated connective tissue corpuscles upon it.

The vessels of the cortex lie in channels—the perivascular channels of His. Numerous delicate fibrillar processes which arise from the stellate cells of the cortex traverse this perivascular space and form connection with the arterial sheath. The capillaries of the cortex are of extremely fine caliber (not over 4 μ in diameter) and of less diameter than the red-blood corpuscles. Bevan Lewis says, however, that we must allow for possible shrinking of the vessel by emptying its channel, as well as for a constricting effect of reagent, and that we can scarcely conclude that even these minute ramifications do not permit the passage of the red-blood corpuscle.

2 **Arterioles of the Cortex.**—In his monograph on the structure of the cerebral cortex, Meynert showed that in the cerebral cortex with a large number of arterioles from the broad expansion of pia, all these arterioles were about the same size and entered adjacent portions of the brain tissue. Each one, moreover, represented to a certain degree, an independent circulatory area. This observation led him to the belief that in the mass of tissue supplied by a small number of larger arterial branches it would be quite possible for differences of blood supply to exist simultaneously in adjacent portions of that tissue. From this he inferred that partial functional hyperæmia of separate cortical areas is readily possible and that the so-called cortical areas could be functionally hyperæmic when the other cortical centers were functionally at rest. The blood supply to the brain would in this way be determined by the functional hyperæmia of the areas which were in a state of activity. In the pia mater we have then main arteries with their branchlets and filaments, and a great number of minute arteriole twigs passing at right angles into cortex. These are commonly known as nutrient arteries. In cases of embolism or thrombosis, therefore, not only does the gray matter of the cortex suffer, but also the subjacent white matter, the amount of destruction, of course, depending upon the size of the vessel obstructed and the amount of communication existing between it and its neighbors. Meynert states that the larger branches of the arteries or the surface of the brain do not lie within the pia, but in the sub-arachnoid spaces.

3. **The Venous Circulation.**—The venous circulation within the cranium presents several peculiar features; the blood flows along the longitudinal sinus toward the occiput, and hence its course is opposed in direction to the blood issuing from the cortical veins which open into the sinus in a forward direction. Hence the fact that the blood which enters the brain by ascending arteries reaches the sinuses by ascending veins is made use of to explain the occurrence of thrombosis

in these vessels, the explanation being that their gravitation is opposed to flow of blood. In this way morbid processes affecting the scalp, such as erysipelas, caries, carbuncle, may readily affect intracranial structures by means of the communication with intracranial veins, *e. g.*, those of the nose, the facial through the ophthalmic, the mastoid veins, and the veins of the diploë. Cerebral anæmia is sometimes produced owing to hydrostatic causes as when a person who has been in bed for a long time and whose blood is small in amount is suddenly raised into the erect position. Such a condition is not infrequently attended by loss of consciousness. Liebermeister regards the thyroid gland as a collateral blood reservoir, which empties its blood towards the head during such changes of the position of the body.

4. **Lymphatic System.**—To the study of the lymphatic system of the brain considerable importance is attached, and our knowledge upon this difficult subject may be attributed chiefly to the labors of Obersteiner, Key, Retzius, Schwalbe, Meynert and Bevan Lewis. Obersteiner was the first to define the nature and connections of the lymph channels. Bevan Lewis is, however, to be credited with having given us the latest and most advanced details as to the relationship of the cortical nerve-cells to these lymph channels, both in health and disease. It will perhaps simplify the subject if we diverge for a moment to consider the endocranial fluids in general.

(*a*) MOVEMENTS AND INTER-RELATIONS OF THE ENDOCRANIAL FLUIDS are important factors in the nutrition of the brain. If the brain were surrounded merely by rigid cranial walls, a partial change in the distribution of arterial blood would be conceivable. A functional increase, however, would be possible only upon one of two conditions, viz.: A corresponding collateral arterial diminution, or a transfer of venous blood in the direction of the sinuses. For the first condition Lewis thought it would be difficult to explain an appropriate mechanism. A venous transfer would be altogether too slow and there could not be any continuous action because the propulsion of the venous current, dependent upon the respiratory movements, would give rise to a frequently interrupted flow of venous blood in the brain. The cranial cavity is not entirely filled by the brain, it includes in addition a number of spaces filled with lymphatic fluid. The dura mater is separated from the arachnoid by a comparatively small space which is lined by the endothelium. This space communicates with the lymphatic glands of the neck, and with the sub-dural spaces which do not immediately surround the nerve roots, but do so in common with the arachnoid and are connected with the lymphatic spaces of peripheral nerves. As an example we have the communication between the auditory labyrinth and the sub-dural space through the space which surrounds the auditory nerve. In the tissue of the dura itself there are also lymph spaces which are connected with the subdural space.

(*b*) THE EXPLANATION OF THE SO-CALLED LYMPH CISTERNS is to be found in the relationship of the arachnoid membrane to the pia. They are connected by means of a net-work of threads and trabeculæ of connective tissue and at the base of the brain by means of perforated membranes. At the summit of the convolutions the threads of this net-work are narrower than over the sulci; while at the base of the brain where the subarachnoidal spaces are dilated there may be no trabeculæ. Meynert enumerates the following cisterns which belong to the surface of the cortex: (I) the space of the fossa Sylvii; (II) farther back the cysterna chiasmatis. In the brain cortex all the vessels are inclosed within channels, known as the perivascular channels of His.

These channels are noticeable in hardened sections and most markedly so in cases of atrophy of the cortex.

The study of the lymph connective tissue is of great importance in cerebral pathology, but it is yet to be shown how the individual elements of this system undergo morbid changes and cause alterations in the movements of the lymph.

5. **Cerebro-spinal Fluid.**—The cerebro-spinal fluid in the brain is secreted by the epithelium of the choroid plexus in the lateral, the third and the fourth ventricles, and possibly from the general epithelial linings of these cavities. The fluid is transparent and has a Sp. Gr. of about 1010. The view that the lymph cisterns act as water cushions to minimize the shock to the brain and to compensate for variations in the blood-pressure is supported by the fact that in cases of spina bifida the cerebro-spinal fluid can be readily driven from the spinal cord into the cranial cavity by pressure of the tumor, so that it may be assumed a passage may be as readily effected in the reverse direction.

6. **Quantitative Relation Between Blood and Cerebro-spinal Fluids.**—There is an intimate relation between the amount of cerebro-spinal fluid and blood within the cranial cavity. Formerly it was taught that as the skull is a rigid box, and as the brain substance and its fluid are practically incompressible, no variation in the amount of blood in the brain could be possible. This, however, is now proved to be erroneous. The average quantity of cerebro-spinal fluid within the cranium is about two ounces, and if it be suddenly withdrawn epilepsy or convulsions may be produced, or if it be rapidly increased in amount coma may result. This fluid has also important mechanical functions, protecting delicate parts of the brain from injury, and distributing vibratory impulses. The presence of the cerebro-spinal fluid is, as pointed out by Donders, of great importance in regulating the pressure uniformly when brain movements occur, so that every systolic and expiratory dilatation of the blood vessels is concentrated upon those parts of the cerebral membrane which do not offer any resistance.

b. The Movements of the Brain.

The movements of the brain are of three kinds: (I) Pulsatile movements communicated from the pulsations of the large basal cerebral vessels. (II) Respiratory movements; brain rising during expiration, and falling during inspiration. (III) Vascular elevation and depression, which alternate and are due to periodic dilatation and contraction of the blood vessels. This last is a periodic arterial dilatation regulated by the vaso-motor center and occurring from one to six times per minute. These movements have been investigated chiefly over the fontanelles of children and where the membranes have been exposed by trephining. The advance of the dilatation wave within the rigid cranial walls aids in the establishment of currents of brain fluid whereby metabolic waste products are carried off through the lymphatic fluid. The brain and the fluid surrounding it are subjected to a certain mean pressure which depends upon the blood-pressure within the vascular system. Naunyn and Schreiber showed that cerebral pressure must be slightly less than pressure within the carotid before the symptoms proper to pressure on the brain occur. The vascular wave causes an expansion of the cerebral mass, followed by a contraction.

Meynert concluded that all stimuli acting on the sensorium create vascular movements and disturb the periodic changes in the condition of the vessels and that of the psychic influences which may cause elevation of blood-pressure, the emotions act more readily and bring about a greater change than purely intellectual processes. Great variations of brain pressure are almost constantly attended by symptoms of disturbances of the nutrition of the brain. If the pressure is moderate the symptoms may remain latent or only show themselves as headache, vertigo, weakness or disturbance of the sensory function. During sleep the circulation of the lymphatic fluid in the brain effects the removal of the waste products and this is to a great extent dependent upon the vascular movements of the brain. Burckhardt regards the influence of this vascular wave as far more powerful than that of the respiratory wave. The irregularities of vascular wave movements which occur when the individual is awake indicate that in certain parts of the brain there is an independence of action just as we know it to be the case in reflex arterial constrictions on the surface of the body.

Pulsatory movements originate from the circle of Willis ; the arteries ascend and their currents are directed upward, as is also the case with the venous currents. The arteries at the base are first to enlarge with the blood flow, then the wave passes into all the branches of the vessels. The brain, however, is only able to enlarge concentrically toward the ventricles on account of the resistance offered by the roof of the skull to the swellings of the convolutions. This concentric swelling of the brain is almost constant and the pressure is neutralized in the ventricles, partly owing to the fact that there is a displacement of cerebro-spinal fluid in the ventricles. When the engorgement of the walls of the ventricles ceases, the blood supply which reaches the cortex through the long arteries is carried downward.

The act of inspiration causes a fall, that of expiration causes an elevation of pulse wave. This influence is most noticeable during forced efforts of expiration and depends upon variations in the venous pressure. As a result of venous pressure, concentric swelling of the hemispheres occurs. The venous pressure acts from the vertex downward instead of from the base upward as does the pulse wave.

2. CONSCIOUS SENSATION, VOLUNTARY MOVEMENTS, MEMORY, REASON.

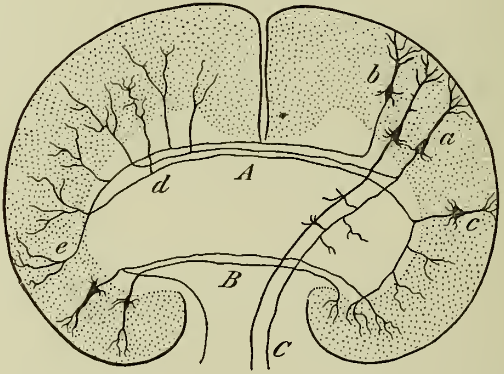
THE PHYSIOLOGY OF THE CEREBRUM.

a. General Consideration.

We have already briefly discussed the actions which an animal is capable of, when all the centers above the medulla oblongata have been removed, and we have endeavored to assign to the medulla oblongata and cord the functions proper to each. In a similar manner the functions of all the parts of the encephalon may be determined by a study and analysis of the various forms of activity which are manifested by animals from which all centers situated in advance of the optic thalami and optic lobes have been removed.

When we turn from the consideration of these facts themselves to the theory of their explanation we enter on a vexed question in physiology. One fundamental fact seems, however, indisputable and established, viz.: *That in the absence of cerebral hemispheres, the lower centers are of themselves incapable of originating active manifestations of any kind.* When the hemispheres are removed all the actions of the animal become the immediate and necessary response to the form and intensity of the stimulus communicated to its afferent nerves. Without such excitation from without the animal remains motionless and inert. It is true that some of the phenomena would seem opposed to this view, but this is only in appearance, not in reality. Thus a frog may occasionally move its limbs spontaneously and a bird may yawn, shake its feathers, or change the foot, but these actions are the result of impressions arising from cutaneous irritation caused by the wounded surface resulting from the operation. The relation between the cerebrum and the sensory and motor tracts is shown and described in some detail in Plates IV. and V. The reader will find it profitable at this point to make a careful study of these plates, also of figures 291, 292 and 293.

Fig. 291.



Transverse section of the cerebrum, showing the probable disposition of the commissural and projection-fibers. *A*, corpus callosum; *B*, anterior commissure; *C*, pyramidal pathway formed of the projection-fibers. (Cajal.)

If we inquire into the nature of the processes which immediately precede this responsive activity, we are led to ask, are these actions merely reflex or are they accompanied by sensation? If we define sensation as the consciousness of impression, it will be seen that the problem which confronts us for solution is whether there is a consciousness accompanying the acts of these animals that are minus their cerebral hemispheres, in other words are these animals, under the conditions of the experiments, capable of psychic activity?

If we were to accept without question the metaphysical view, the answer would not be difficult, viz.: that abolition of the hemi-

PLATE IV

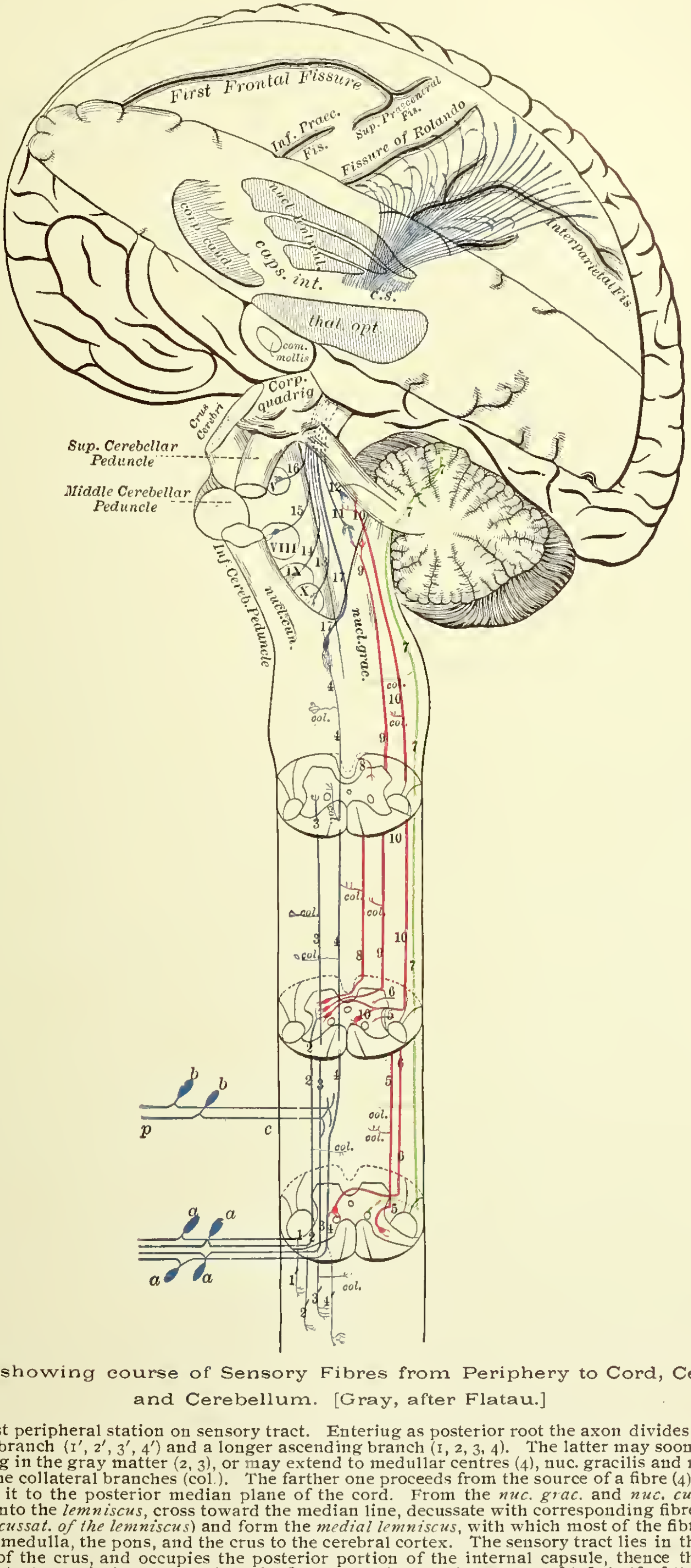


Diagram showing course of Sensory Fibres from Periphery to Cord, Cerebrum and Cerebellum. [Gray, after Flatau.]

a. First peripheral station on sensory tract. Entering as posterior root the axon divides into short descending branch (1′, 2′, 3′, 4′) and a longer ascending branch (1, 2, 3, 4). The latter may soon terminate by arborizing in the gray matter (2, 3), or may extend to medullar centres (4), nuc. gracilis and nuc. cuneatus. Note the collateral branches (col.). The farther one proceeds from the source of a fibre (4) the nearer will he find it to the posterior median plane of the cord. From the *nuc. grac.* and *nuc. cuneatus* the axons pass into the *lemniscus*, cross toward the median line, decussate with corresponding fibres of opposite side (*Decussat. of the lemniscus*) and form the *medial lemniscus*, with which most of the fibres proceed through the medulla, the pons, and the crus to the cerebral cortex. The sensory tract lies in the tegmental portion of the crus, and occupies the posterior portion of the internal capsule, thence through the corona radiata to cortical areas outlined in figure showing mesial aspect of left half of the brain of *Macacus* The collateral branches give rise to secondary sensory tracts, but the one outlined is the most important.

PLATE V.

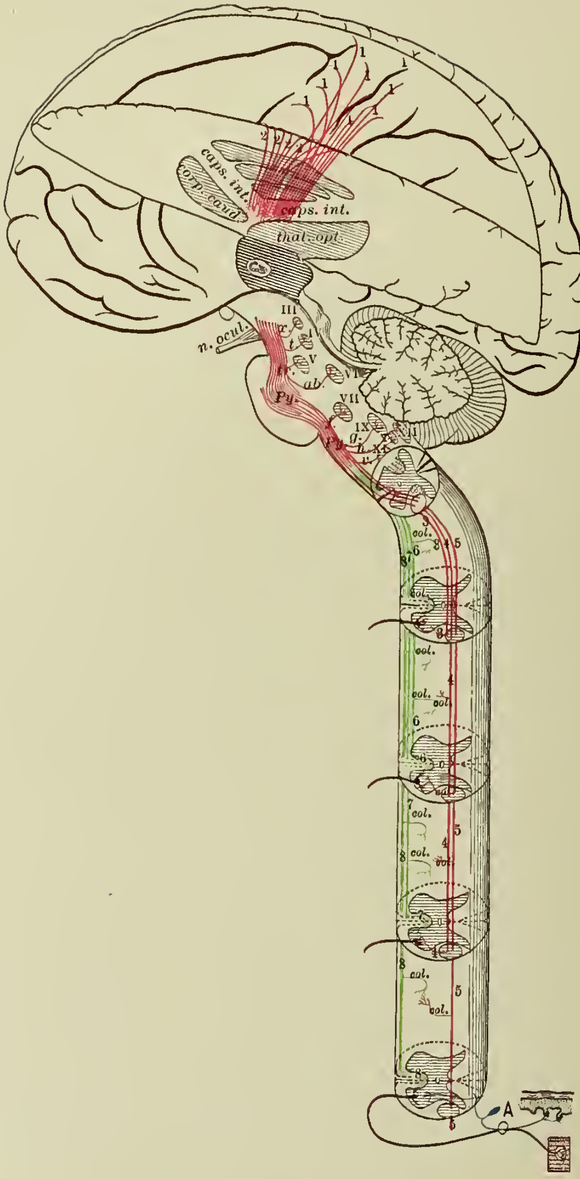
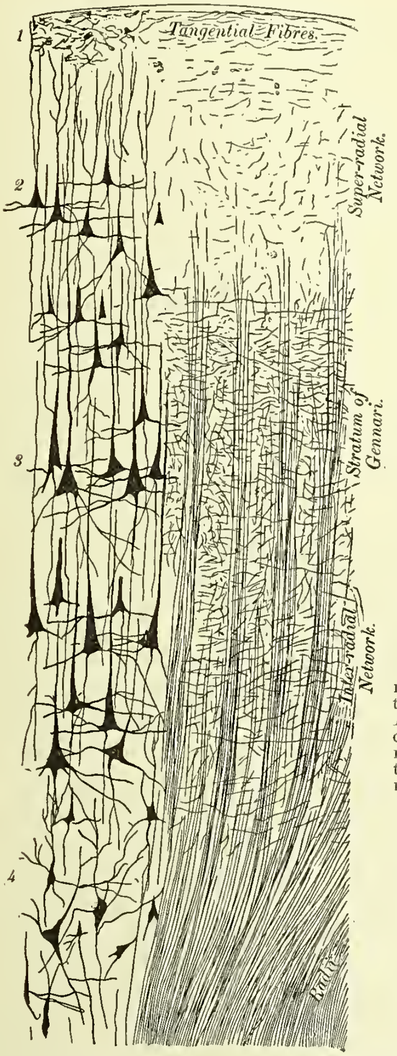


Diagram showing course of Motor Fibres from the Cerebrum and Cord to the Periphery. [Gray, after Flatau.]

The motor impulses proceed from the pyramidal cells of the motor area of the cortex to the pyramidal fibres, via the corona radiata to the motor nuclei of the cranial and the spinal nerves, the former lying in the brain stem and the latter in the anterior horns of the spinal cord. Note that the motor fibres lie anterior to the sensory in the internal capsule (Compare Plate IV.), and that they pass into the crura cerebri lying in the most ventral portion in what is known as the *Pes*, thence through the pons and medulla, where they are visible as two compact bundles, *the pyramids* (Py). At the lower end of the medulla, in the region of the first and second cervical nerves, there is a *decussation* of the *pyramids*, one portion of each pyramid decussates and passes down the cord in the *lateral pyramidal column*, while the other passes without decussating down the *anterior pyramidal column* or *column of Türck*. Note that collaterals from the fibres of the column of Türck, pass to the opposite side of the cord through the anterior commissure to motor cells of opposite side; so that eventually all of the motor tract crosses to the opposite side, where they arborize around motor cells of the anterior horns. The axons from these cells pass out the anterior roots and are distributed to muscles and glands.

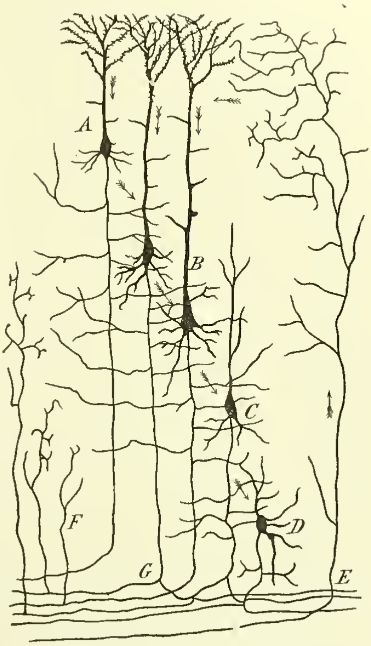
spheres abolishes certain fundamental powers of mind, that the functions of the lower centers lie outside of the sphere of the mind proper. But this way of looking at the subject does not harmonize with known physiological facts. It is known that areas may be cut away from the hemispheres involving the territory of intellectual consciousness without interfering with consciousness; the will may be abolished while consciousness remains. Hence we are not entitled to say that mind as a unit has a local habitation in any one part of the encephalon but rather that mental manifestations depend on the conjoint action of several parts. If we

FIG. 292.



Human cortex stained with Weigert's hæmatoxylin on the left, and by Golgi's method on the right.

FIG. 293.



Probable direction of the currents and the nervous protoplasmic connections in the cell of the cerebral cortex. *A*, small pyramidal cell; *B*, large pyramidal cell: *C*, *D*, polymorphous cells; *E*, terminal fiber coming from other nerve-centers; *F*, collaterals of the white matter; *G*, axis-cylinder bifurcating in the white matter. (CAJAL.)

study the nervous results which are brought about by external stimulation of animals it will be found impossible to determine how far the element of consciousness enters into the reaction. Thus a severe pinch on the tail or foot of a brainless rabbit elicits, not merely convulsive reflex movements, but calls forth a repeated and prolonged cry which is characteristic of pain. But may it not be that the mesencephalon is a center of reflex action of a special form, differing from the spinal cord not in kind, but in degree of complexity? Just as the medulla oblongata is a more highly specialized and complex center than the spinal cord, so the mesencephalon may be the center of still more highly specialized reflex action. Hence the plaintive cry may be purely a reflex phenomenon, not depending on any true sense of pain.

b. Localization of Functions in the Cerebrum.

The phenomena of disease throw light on this question; for example, if a disease can occur which will practically detach the cerebrum from the mesencephalon and leave thought and speech intact we may expect to collect symptoms and testimony which will point to the location or localization of the consciousness of impressions. If the crus cerebri or the posterior part of the internal capsule be diseased, which are not uncommon occurrences in clinical experiences, the individual has absolutely no consciousness of tactile impressions made on the opposite side of his body. In the mesencephalon alone therefore sensory impressions are not correlated with modifications of consciousness; hence we must conclude that sensation is a function of the higher centers. We may conclude from the homology of the mesencephalon of man with that of the lower vertebrates that all are of the same type and only differ in degree of independence.

The following words of Herbert Spencer (Principles of Psychology, 1870) contain the pith of our knowledge with reference to special location of mental action: "Whoever calmly considers the question cannot long resist the conviction that different parts of the cerebrum must in some way or other subserve different kinds of mental action. The different parts of the cerebrum do subserve different kinds of mental action, but they only subserve, and we cannot as yet determine where or how the different kinds of mental action are ultimately served." Further, Herbert Spencer says: "Localization of function is the law of all organization whatsoever, and it would be marvelous were there here an exception. Either there is some arrangement, some organization in the cerebrum or there is none. If there is no organization the cerebrum is a chaotic mass of fibers incapable of performing any orderly action. If there is some organization it must consist in the same physiological division of labor in which all organization consists, and there is no division of labor physiological or other, but what involves the concentration of special kinds of activity in special places."

It has already been learned from the facts of human physiology and pathology that consciousness is inseparable from the activity of the cerebral hemispheres, and that therefore, however much the responsive actions of the lower ganglia may resemble conscious actions, they do not come within the sphere of truly physical phenomena.

Up to a recent date, the results of experimental physiology and human pathology had been considered as opposed to the localization of special functions in distinct regions of cerebral hemispheres. Many unquestionable facts of clinical medicine, however, such as limited paralysis in connection with limited cerebral lesions, appeared wholly inexplicable except on the hypothesis of a differentiation of function in the cerebral hemispheres. In more recent times established coincidence of aphasia or loss of speech, with disease of a certain region in the left hemisphere, served still further to cause thoughtful students of this subject to seek rational explanations upon the basis of a differentiation of function in the cerebrum.

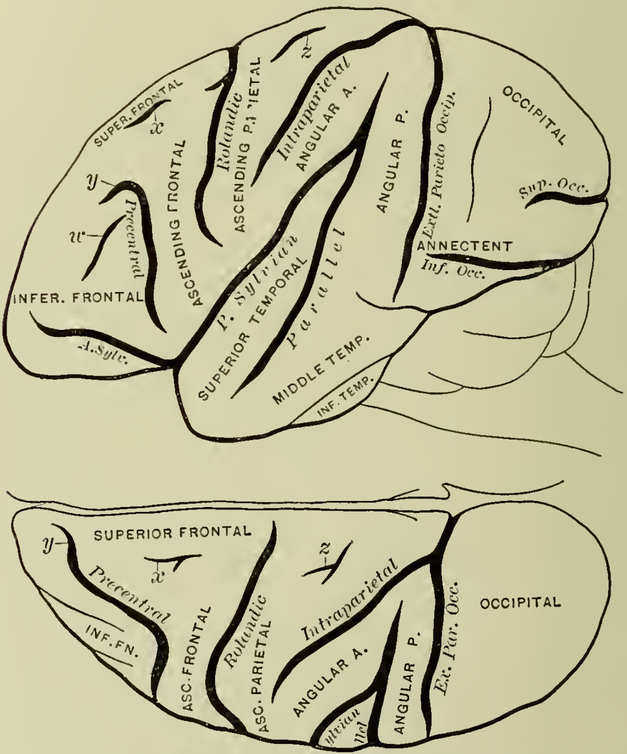
Hughlings Jackson from a minute and careful study of the phenomena of unilateral and limited epileptiform convulsions arrived at the conclusion that they were due to irritation or discharge of energy from certain convolutions of the opposite cerebral hemisphere, functionally related to the corpus striatum and muscular movements. Though he furnished many arguments in favor of this hypothesis, since verified, his views were regarded, at the time, as merely ingenious speculations and devoid of any actual proof that the gray matter of the convolution was really excitable. Experimental physiologists had all failed to obtain evidence of the susceptibility of the cerebral cortex to any of the ordinary stimuli of nerves, mechanical, chemical, thermal or even electrical. This apparent inexcitability of the cerebral cortex greatly retarded the progress of cerebral physiology.

A new era in cerebral physiology was inaugurated by the discovery by Fritsch and Hitzig in 1870 that the application of the galvanic current to the surface of the cerebral hemisphere in dogs gave rise to movements on the opposite side of the body—movements which varied with the position of the electrodes.

The phenomena of localized and universal convulsive movements, attributed by Hughlings Jackson to vital irritation of certain regions of the cortex, are precisely of the same nature as those induced by electrical irritation of the same regions. The great and significant feature of the reactions produced by electrical excitation of the cortex is that they are definite, may be predicted and vary with the position of the electrodes. So, as will be seen later, areas in close proximity to each other, separated only by a few millimeters or less, react to the electrical current in a totally different manner. If there were no functional differentiation of the areas under stimulation the diverse effects would be absolutely incomprehensible on any theory of mere physical conduction. Movements of the limbs can only be excited from certain points, all others being ineffective.

1. **Experiments upon Monkeys.**—The surface of the cerebral hemispheres in monkeys is divided into certain lobes and convolutions by primary and secondary fissures. The general arrangement of these varies somewhat from that of the human brain; however the homologies may be traced with fair accuracy, and the results obtained from experiments are indicative of the func-

Fig. 294.



Outline of brain of monkey (*Macacus*) to show principal sulci (fissures) and gyri (convolutions). Natural size. Over each sulcus, purposely printed very thick, the name is written in *italics*, over each gyrus in SMALL CAPITALS. *x* indicates the small depression, hardly to be called a sulcus, which is supposed to be homologous with the superior frontal sulcus of man; and *w*, *y*, *z*, similarly indicate sulci whose homologies are not certain. (FOSTER after HORSLEY and SCHAEFER.)

PLATE VI.

FIG. 1.

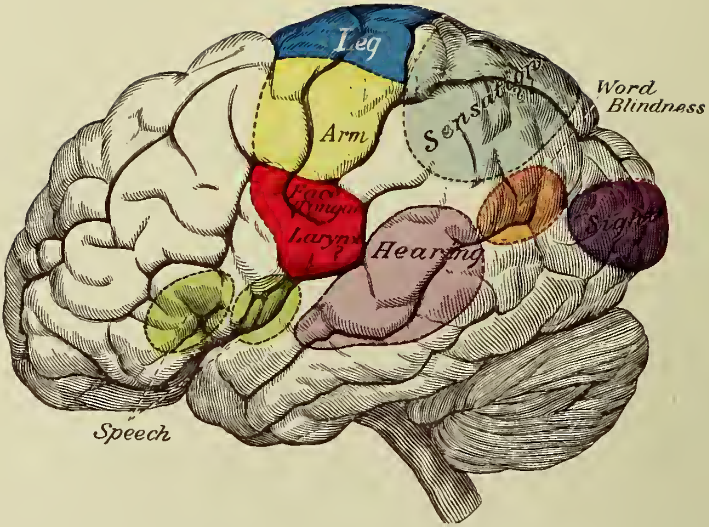


Chart of Localization of Cortical Centres Determined on External Surface of Cerebrum. (Gray.)

FIG. 2.

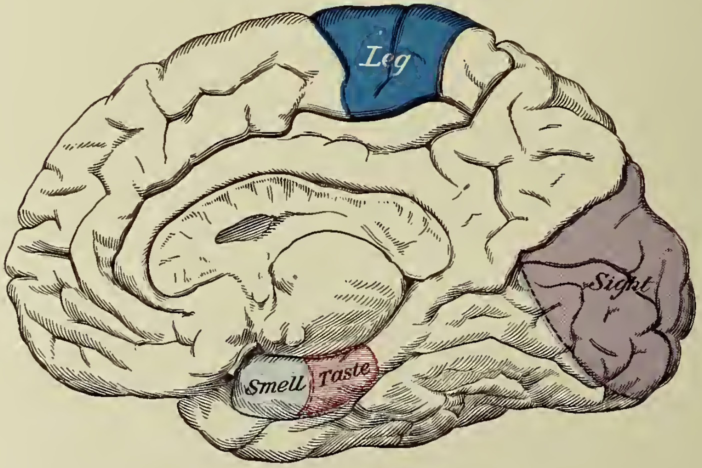


Chart of Localization of Cortical Centres Determined on Medial Surface of Cerebrum. (Gray.)

tions of homologous areas of the human brain. Electrical stimulation of certain areas gives rise to definite response. The following are the principal phenomena usually observed:

(*a*) Stimulation of the upper portion of the ascending parietal lobule causes the opposite hind limb to be advanced as in walking, the thigh being flexed on the pelvis, the leg extended, the foot flexed and the toes spread and extended. (See Figs. 294 and 295.)

(*b*) On the upper extremity of the ascending parietal and adjoining portion of the ascending frontal convolution: Flexion with outward rotation of the thigh, rotation inwards of the leg with flexion of the toes.

(*c*) On the ascending frontal convolution, at the base of the superior frontal: Extension forwards of the opposite arm as if the animal tried to reach and touch something in front.

(*d*) On the ascending frontal convolution at the bend of the knee of the præcentral sulcus: Flexion and supination of the forearm.

(*e*) On the ascending frontal convolution below 4: Retraction and elevation of the angle of the mouth.

(*f*) On ascending frontal convolution below 5: Elevation of the ala of nose and upper lip.

(*g*) On the lower extremity of the ascending parietal convolution: Opening of the mouth with protrusion and retraction of the tongue.

(*h*) On the lower extremity of the ascending parietal convolution: Retraction of the angle of the mouth.

(*j*) On the superior temporal convolution: Pricking up of the opposite ear, turning of the head and eyes to the opposite side, dilatation of the pupils.

(*k*) Stimulation of the central lobe, or Island of Reil causes no motor reactions.

(*l*) Stimulation of the occipital lobe causes no motor reaction.

(*m*) Horsley and Beevor have made important contributions to the physiology of the mesial aspect of the brain. They found that the marginal convolution—located above the calloso-marginal fissure—is excitable throughout, except in the præ-frontal region (F. R., Fig. 296). The figure shows the results obtained by the experimenters referred to.

2. **The Results of Observations upon Man.**—Clinical observation has enabled us to determine with considerable accuracy the outline of motor and of sensory areas on the cortex of the human brain. A comparison of Plate III. with Fig. 252 will show that the motor area of the human cerebral cortex is located, like that of the monkey, upon either side of the fissure of Rolando on the lateral aspect of the cerebrum and upon the posterior por-

tion of the marginal convolution on the mesial aspect of the cerebrum. For obvious reasons the determination within the motor area of minute fields which serve as centers for voluntary control of limited groups of muscles has not advanced as far in the human subject as in the monkey. On the other hand, and for reasons just as obvious, the determination of the location and outlines of sensory and speech areas has progressed much farther in man than in the monkey.

We have now traced sensory impressions to the cerebral cortex, to the sensorium ; we have found how one cortical portion communicates with another, and we have traced motor impulses from the cortical centers of voluntary motion, through the pons, medulla and cord to the muscles. It will be seen that sensation followed by a responsive voluntary motion is analogous to a reflex act, differing from it only in the presence of *consciousness of the process.*

c. The Higher Cerebral Functions.

It is not within the province of this brief manual to discuss the higher cerebral functions or the intellect of man. For a treatment of this subject the student is referred to the various works on psychology.

Innumerable clinical observations make it certain that the physical basis of the mind of man is the cerebral cortex. That certain attributes of the mind are lost with the functional destruction of certain portions of the cortex indicates that the localization of function is not confined to sensation and to volition.

Through the interrelation and interaction of cerebral centers one is not only conscious of sensation, but he interprets the sensation, referring it to some object outside of the brain itself. Such an interpretation of sensation is called *Perception.*

Sensations and perceptions affect the brain structure in some mysterious way leading to a retention of the impression, with ability on the part of the subject to call up the impression again : *Memory* and *Recollection.*

Through the aid of the memory a series of sensations and perceptions may be combined, into a clear mental picture : *Conception.*

Conception merges into *Imagination,* for the latter is the "power of the mind to create mental pictures out of the data derived from experience." These mental pictures may either be faithful reproductions of previous sensations and perceptions : *Representative imagination* (Conception) ; or it may construct entirely new pictures combined from various elemental sensations and perceptions : *Constructive imagination,* or *Imagination proper.*

Given the powers enumerated and defined above the mind is able to make a series of judgments or conclusions, *i. e.,* to *Reason.*

As a result of reason the subject may deliberately enter upon a certain line of action. The power of the mind *to will to do* is called *Volition or The Will.*

Sensations though the medium of memory may call forth in the mind a series of *Emotions*: fear, anger, love, hatred, etc.

CHAPTER XII.

THE PHYSIOLOGY OF THE MUSCULAR SYSTEM.[1]

A. GENERAL ACTIVITIES OF MUSCULAR TISSUE.

B. ENUMERATION AND CLASSIFICATION OF THOSE MUSCULAR ACTIVITIES ARISING FROM A CHANGE IN FORM.

1. THE INVOLUNTARY MUSCLES.
2. THE VOLUNTARY MUSCLES.
    - *a.* MUSCULAR ORGANS: THE TONGUE.
    - *b.* MUSCLE-BONE ORGANS: THE SKELETAL MUSCLES.
        - (1) *General Functions of Muscle-bone Organs.*
        - (2) *Special Functions of Muscle-bone Organs.*
        - (3) *Animal Mechanics.*

C. SPECIAL MUSCULAR ORGANS: THE LARYNX.

1. SUMMARY OF THE ANATOMY OF THE LARYNX.
    - *a.* THE SKELETON OF THE LARYNX.
    - *b.* THE MUSCLES OF THE LARYNX.
    - *c.* THE INNERVATION OF THE LARYNX.
2. THE MECHANICS OF THE LARYNX.
    - (1) *The Abduction of the Glottis.*
    - (2) *The Adduction of the Glottis.*
    - (3) *The Tension of the Vocal Cords.*
    - (4) *The Levers of the Larynx.*
3. THE ACOUSTICS OF THE LARYNX.
4. THE VOICE: PHONATION.
    - *a.* SPEECH.
    - *b.* SONG.

THE PHYSIOLOGY OF THE MUSCULAR SYSTEM.

A. GENERAL ACTIVITIES OF MUSCULAR TISSUE.

UNDER the influence of the nervous system various chemical, thermal, electric and morphotic changes occur in constant succession in muscle tissue. In our study of metabolism we found that in this tissue the most active metabolic changes take place. Even when a muscle is said to be resting, *i. e.*, not undergoing morphotic changes, the metabolism within the tissue may be very active.

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[1] Introductory to this subject review, under *General Physiology*, the topics: "*Motion*" and "*Contractility.*"

(*a*) CHEMICAL CHANGES.—Under general metabolism we found that muscle tissue is the scene of important chemical changes. Most important among these changes is the oxidation of dextrose, with the attendant consumption of oxygen and liberation of CO_2 and H_2O. The katabolism of energy-producing ("circulating") proteids must now be recalled. The result of this katabolism is the formation of nitrogenous (kreatin, etc.) and non-nitrogenous molecules of simple structure ($CO_2 + H_2O$, etc.). Next in importance is the destructive metabolism of muscle protoplasm. Incident to this katabolism oxygen is consumed and CO_2, H_2O and a nitrogenous molecule,—kreatin, for example,—are liberated. Recent investigations in this field make it certain that a part at least of the carbon, hydrogen and oxygen liberated in muscle katabolism takes the form of sarco-lactic acid,—$CH_3\cdot CHOH\cdot COOH$,—which gives the acid reaction to fatigued muscle.

(*b*) THERMAL CHANGES.—Incident to the katabolic changes just enumerated energy must be liberated. This energy may take different forms. In a resting muscle the energy is liberated in the form of heat. Recall the fact that the muscle-tissue is the tissue of thermogenesis. It is probable that in simple thermogenesis the katabolism involves almost exclusively the dextrose and "circulating" or energy-producing proteids leaving the muscle protoplasm unimpaired. The thermogenetic activity of muscle-tissue is under the direct control of thermogenetic centers in the brain.

(*c*) ELECTRIC CHANGES.—Katabolism of muscle-tissue and of circulating nutrients within muscle-tissue is always attended with the liberation of heat-energy. It may or may not be attended with the liberation of electric energy. It seems fairly well established that electric changes manifest themselves only when the muscle contracts (The current of injury—demarkation current—excepted). That part of the muscle where the contraction wave begins is electro-negative to that part of the muscle yet uninfluenced by the contraction wave. In the beating heart the base is electro-negative to the apex when the systole begins, and at the end of systole the apex is electro-negative to the base.

(*d*) CHANGES OF FORM.—One of the forms of energy liberated in muscle metabolism is mechanical energy. Mechanical energy manifests itself by moving matter through space. In the locomotion of an animal mechanical energy is manifested. Animal locomotion in higher animals is performed by use of the skeletal structures as levers. The levers are set in motion by the tension of muscle-tendons. This tension is possible only as a result of a *change* of *form* of the muscle. The muscle contracts by increasing its lateral dimensions at the expense of its longitudinal dimensions. This brings the origin and insertion of the muscle nearer together. If the origin of the muscle is a fixed point, tension will be exerted upon the insertion. Thus the change of form of muscles makes it possible for them to perform mechanical work as one of the manifestations of the energy liberated in muscle metabolism.

B. ENUMERATION AND CLASSIFICATION OF THOSE MUSCULAR ACTIVITIES ARISING FROM CHANGE IN FORM.

1. THE INVOLUNTARY MUSCLES.

a. Non-Striated Involuntary Muscles.

(*a*) CHARACTER OF CONTRACTION.—Slow, somewhat prolonged and relatively weak. *Examples:* (I) Peristaltic contraction of walls of alimentary canal and of ducts of associated glands. (II) Contraction of bladder in act of micturition. (III) Contraction of walls of blood vessels. (IV) Contraction of uterine walls in act of parturition. (V) Contraction of ciliary muscles in act of accommodation. (VI) Contraction of the *erector pili* muscles in "*Cutis anserina.*" (VII) Contraction of gland-ducts in general.

(*b*) MECHANICS OF MOVEMENTS PRODUCED BY UNSTRIPED MUSCLE.—In examples (I), (II), (III), (IV) and (VII), the walls of the cylindrical or subspherical organs in question, contract upon the more or less fluid contents of the organs. There is no leverage and no antagonistic muscular action. The contraction produces pressure of the wall toward the center of the enclosed space. The pressure is equal upon all equal areas of the wall and the tendency is to drive the liquid contents toward the direction of least resistance, toward the physiological outlet of the cavity. In examples (V) and (VI) the muscles contract against the elasticity of certain tissues which oppose their action. During relaxation of the muscle the elasticity of the tissues restores the relations of the tissues to their usual position.

b. Striated Involuntary Muscle.

(*a*) THE HEART IS A STRIATED INVOLUNTARY MUSCLE.—The *contractions of the heart are peristaltic in character.* Though peristalsis is somewhat obscured in the heart-action in higher vertebrates one has only to refer to the action of that organ in lower vertebrates or in the embryonic life of higher vertebrates to be convinced of the truth of the statement. The character of the contractions of heart-muscle differs very much from that of other involuntary muscles: first, in the rapidity of the contractions; and second, in the force of the contraction. It is probable that the striation is the effect of this difference of action rather than its cause.

(*b*) The mechanics of the heart-action are of the same order as in the examples cited above, being a contraction of the walls of a hollow organ upon the contents expelling them in the direction of least resistance.

2. THE VOLUNTARY MUSCLES.

a. Muscular Organs: The Tongue.

A purely muscular organ like the tongue of one of the higher animals, the proboscis of the elephant or the prehensile upper lip of the horse and allied animals, notably the tapir, present the most perfect types of universal motion in the animal economy. The tongue may be lengthened or shortened, raised or lowered, swept from side to side, or circumducted at will. The highly mobile and prehensile tongue of the cow may even present various combinations of these movements in different portions of the tongue. The movements may be rapid and strong. From the standpoint of mechanics the tongue represents a flexible lever of the third class whose fulcrum is the base of the tongue and whose weight may be represented by the tip. The power is applied between the fulcrum and the weight by the contraction of the muscles on one side of the lever to turn the tip in that direction. The central portion of the lever would be represented by the relaxed muscles on the convex side of the tongue.

b. Muscle-bone Organs: The Skeletal Muscles.

Muscle alone or bone alone could not accomplish locomotion or any of the general movements of the body. A locomotory organ among the vertebrates has two essential components . viz., muscle and bone. The so-called skeletal muscular system is a system composed of *muscle-bone organs.*

1. **The General Functions of Muscle-Bone Organs.**—(*a*) Flexion and Extension are terms applied to the bending and the unbending of segments of the body or of its appendages. For example, the forearm may be flexed upon the upper arm, and then straightened out or extended. The fingers are flexed when one grasps an object and extended when one releases the object. The thigh may be flexed upon the abdomen ; the leg may be flexed upon the thigh and the foot may be flexed upon the leg.

(*b*) Adduction and Abduction are terms applied to the carrying of arms or legs toward or away from the median ventral plane of the body.

The confusion which exists in the application of some of these terms, especially of abduction, adduction, flexion and extension of arm, necessitates their further illustration. To that end let us recall the general disposition of the muscle-bone organs in a typical mammal. (See Fig. 295.)

Adduction is the bringing of the femur or humerus toward the median ventral plane of the body or the bringing of a digit toward the axis of the pes or the manus. Abduction is motion in the opposite direction. Man in his erect position with the arms held in the horizontal plane laterally may bring them toward the median ventral plane, keeping them in the horizontal plane—*Ventral Adduction* of the *Humerus*—or he may bring them to the same median plane above the head—*Anterior Adduction* of the *Humerus*—or he may bring them down to the sides—*Lateral Adduction* of the *Humerus*. In a similar manner there may be *Posterior* and *Ventral Adduction* of the *Thigh* or *Femur*, but, except in the case of contortionists, the hip joint will not admit of lateral adduction. When the typical mammal stands upon all-fours the anterior and posterior extremities of one side define a ventral plane. In flexion the femur moves anteriorly in that plane until, in extreme flexion, it rests upon the abdomen. The humerus in flexion moves posteriorly in the vertical plane until, in extreme flexion, it rests against the thorax or slides along the thoracic wall until its axis approaches or even passes a line parallel to the axis of the body. In man, when in the erect position, with the arms extended horizontally in front (ventrally) and parallel to each other, the arms would be flexed upon the body by bringing them down to the thoracic walls, keeping them in the vertical plane throughout the movement.

FIG. 295.

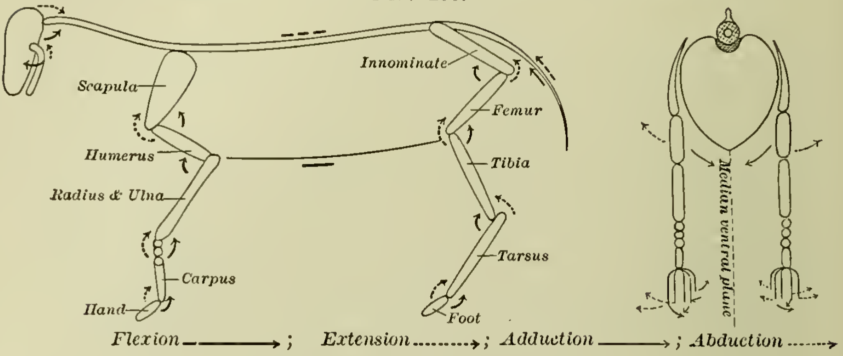

Diagram of typical mammalian skeleton.

(*c*) ROTATION.—Certain joints, notably the ball-and-socket joints at the proximal extremities of humerus and femur, admit of a rotation of the limb about its axis. If one rests the weight upon the heel the toe may be swung to right or left through an angle of about 90°. It is neither the ankle-joint nor the knee-joint which moves in this case, but the hip-joint, the head of the femur rotating readily within the acetabulum of the innominate bone. In a similar way the arm may be rotated upon its axis through the rotation of the head of the humerus in the glenoid cavity of the scapula. Another rotating articulation is found between the two bones of the forearm; the radius, rotating upon the external condyle of the humerus, is thrown obliquely across the ulna in *pronation* and drawn back parallel to the ulna in *supination*. Under the head of rotation one may enumerate: (I) rotation proper; (II) pronation and supination.

(*d*) CIRCUMDUCTION.—All joints which are subject to the four motions, flexion, extension, adduction and abduction, are subject also to the movement called *circumduction*. One may swing the arm or the leg around in a circle; this is circumduction, and it is clearly a combination of the four motions just enumerated. The muscles and nerves involved in such a motion are simply a combination of those involved in the four primary movements taken together.

What muscles are involved in the above enumerated functions? What is the innervation of the muscles? Through which spinal nerve does the innervation come? Opposite which spinous process is the deep origin of the enumerated nerves? Whence comes the blood-supply of the muscles? All of these questions are of importance to the clinician. They are briefly answered in the following table, the data for which have been taken from Quain, Edinger and Gowers:

2. **Special Functions of Muscle-bone Organs.**—(*a*) MOTIONS OF THE CRANIUM UPON THE SPINAL COLUMN.

FUNCTION.	MUSCLE.	INNERVATION.	NERVE ROOT.	SEGMENT OF CORD.
Flexion	Rectus Cap. Ant. Maj.	Suboccipital	I C	Bet. Occ. & At.
	Rectus Cap. Ant. Min.	"	I II C	Bet. Ax. & Atl.
	Sterno-Cledo. Mast.	Spinal Accessory	XI Cran	Jug. Foram.
		Deep br. of Cerv. Pl.	II C	Body 2d Cer.
Extension.	Rectus Cap. Post. Maj.	Suboccipital	1 C	Bet. Occ. & At.
	Rectus Cap. Post. Min.	"	"	" " " "
	Sup. Oblique	"	"	" " " "
	Complexus Bivent.	"	"	Bet. Ax. & Atl.
		Gt. Occipital	II C	Opp. body 2 C.
		Int. Br. Post. Div. Cer.	6–7–8 C	Opp. 4–5–6 C. Sp.
	Splenius Cap. Colli	Ext. Br. Post. Div. Cer.	2–3 C	Bet. Ax. & At.
	Upper seg. Trapezius	Spinal Accessory.	XI Cran	Jug. Foram.
		Ant. Div. 3–4 C.		Opp. 1–2 C. Sp.
Abduction and Adduction.	Recti Lateralis	Suboccipital	I C	Bet. Oc. & At.
	Assisted by: Trapezius	Spinal Accessory	II C	Jug. Foram.
		Ant. Div. 3–4 Cerv.	3–4 C	Op. 1–2 C. Sp.
	Splenius	Ext. Br. Post. Div. Cer.	2–3 C	Op. Bod. 2 [1 C. Sp.]
	Complexus Bivent.	Suboccipital	1 C	Bet. At. & Ax.
		Gt. Occipital	2 C	Opp. Bod. 2 C.
		Int. Br. Post. Div. Cer.	6-7-8 C	Op. 4, 5, 6 C. Sp.
	Sterno-Mastoid	Spinal Accessory	II C	Jug. Foram.
		Deep Br. Cer. Plex.	2 C	Opp. Bod. 2 C.
Rotation.	Sterno Mastoid	Deep Br. Cerv. Plex.	2 C	Op. Bd. 2 C.
	Compl. Biv. of one side acting with it.	Suboccipital	1 C	Bet. At. & Ax.
		Gt. Occipital	2 C	Op. Bd. 2 C.
		Int. Br. Post. Div. Cer.	6–7–8 C	4–5–6 C. Sp.
	Rect. Cap. Ant. Maj.	Suboccipital	1 C	Bet. At. & Ax.
	Splenius	Ext. Br. Post. Div. Cer.	2–3 C	Op. Bd. 2 C. [1 C. Sp.]
	Trachelo Mast.	"	"	" "
	Rect. Cap. Post. Maj.	Suboccipital	1 C	Bet. At. & Ax.
	Inf. Oblique	"	"	" "
		Gt. Occipital	2 C	Op. Bd. 2 C.

(*b*) Movements of Upper Arm.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion	Latissimus Dorsi	L. Subscapular	7 C	Bet. 5–6 C. Sp.	Axillary
	Teres Major	Subscapular	7 C	Bet. 5-6 C. Sp.	"
	Post. Seg. of Delt.	Circ. Br. Cerv. Pl.	4–5 C	Op. 2–3 C. Sp.	Post. Circum.
	Coraco-brach.	Musculo Cutan.	5–7 C	Op. 3 C. Sp.	Brachial
Extension.	Pectoralis Maj.	Ant. Thr. Br. C. Pl.	7 C	Bet. 5–6 C. Sp.	Axillary
	Ant. & Mid. Sg. Del.	Circumflex	4–5 C	Bet. 2–6 C. Sp.	Ant. Circum.
	Coraco-brach.	Musculo Cutan.	5–7 C	Op. 3 C. Sp.	Brachial
	Supra-Spinatus	Supra-scapular	5–6 C	Bet. 4–5 C. Sp.	Post. & Supra Sp.
Lateral Adduc'n.	Pect. Maj. low ⅓	Ant. Thoracic	7 C	Bet. 5–6 C. Sp.	Axillary
	Latissimus Dorsi	L. Subscapular	7 C	"	"
	Teres Maj.	Musc. Br. Subsc.	6–7	"	"
	Long Hd. Triceps	L. Br. Circum.	4–7 C	5–7	"
	Coraco-brach.	Musculo Cutan.	5–7 C	4–5–6	Brachial
Lat. Abd.	Ant. & Mid. Sg. Del.	Upper Br. Circum.	4–5 C	Bet. 2–6 C. Sp.	Circumflex
	Supra-spinatus	Supra-scapular	5–6 C	5–6	Post. Supra Sp.
	Infra-spinatus	" "	5–6 C	5–6	" "
Ventral Adduc'n.	Pect. Maj. Upper Pt. until horizontal then low pt. acts	Ant. Thoracic External and Internal	7 C	Bet. 5–6 C. Sp.	Axillary
	Subscapularis	Subscapular	4–8 C	Bet. 5–6 C. Sp.	Subscapular
	Coraco-brachialis	Musculo Cutan.	5–7 C	5–6	Brachial
Ven. Abd.	Post. Seg. Deltoid	Sup. Br. Circum.	4–5 C	Bet. 2–6 C. Sp.	Post. Circum.
	Infraspinatus	Supra-scapular	5–6 C	5–6	Subscapular
	Teres Minor	Br. of Circum.	4–5 C	5–7	Axillary

(*c*) Movements of Forearm.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion.	Biceps	Musculo Cutaneous	5–8 C	Op. 3 C. Sp.	Brachial
	Brachialis Ant.	Br. Musculo Spiral	4–8 C	Bet. 3–6 "	Brachial
		Br. Musculo Cutan.	"	Op. 3 "	Brachial
	Supinator Long	Br. Musculo Spiral	"	Bet. 3–6 "	Radial
	Flex. Carp. Rad.	Br. Musc. Sp. Med.	"	3–6 "	Radial
	Flex. Carp. Ulnar	Ulnar.	8 C 1 D	Op. 6–7 "	Ulnar
	Flex. Sub. Dig.	Musc. Br. Median	4–8 C	Bet. 3–6 "	Ulnar & Med.
Extension.	Triceps	Musculo Spiral	4–5 C	Bet. 3–6	Brachial
	Anconeus	" "	"	3–6	Brachial
	Ext. Carp. Rad. Long	" "	"	3–6	Radial
	Ext. Carp. Rad. Brev.	Post. Interosseous	"	3–6	Radial
	Ext. Carp. Ulnaris	" "	"	3–6	Ulnar
Supination.	Supinator Long.	Musculo Spiral	4–7 C	Bet. 3–6 C. Sp.	Radial
	Supinator Brev.	Post. Interosseous	"	3–6	"
	Biceps	Musculo Cutaneous	"	3–6	Brachial
	Flex. Carp. Rad.	Median	"	3–6	Radial
Pronation.	Pronator Rad. Ter.	Ant. Thoracic	8 C 1 D	5–6	Rad. & Ulnar
	Pronator Quadratus	Median	5–8 C	5–6	Rad. & Ulnar

(*d*) Movements of the Hand.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion	Flex. Carp. Ulnar	Ulnar	8 C 1 D	Op. 6–7 C. Sp.	Ulnar
	Palmaris Brev.	Median	4–8 C	Bet. 5–6	"
	Palmaris Long.	Median	"	5–6	"
	Finger Flexors	Median & Ulnar	8 C 1 D	Op. 6–7	Ulnar. Rad. Med.
Extension.	Ext. Carp. Rad. Long	Musculo Spiral	4–7 C	Bet. 3–6	Radial
	Ext. Carp. Rad. Brev.	Post. Interos.	"	3–6	"
	Ext. Carp. Ulnaris	" "	"	3–6	Ulnar
	Finger Extensors	" "	"	3–6	Ulnar. Rad. Med.

(*e*) MOVEMENTS OF THIGH.

FUNCTION.	MUSCLE.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion.	Psoas Magnus	1–2 Lumbar	3–4 L	Op. 11 D. Sp.	Ilio Lumb.
	Iliacus	Ant. Crural	6 L	Bet. 11–12	Obt. Glut.
	Adduct. Long.	Obturator	1–4 L	Op. 12	Ob. Gl. Int. C.
	Adduct. Brevis.	Obturator	"	"	" " " "
	Sartorius	Ant. Crural	6 L	Bet. 11–12	Br. Prof. Fem.
	Pectineus	Ant. Crur. & Obt.	Above	Above	Ob. Gl. Int. C.
	Gracilis	Ant. Crur. & Obt.	"	"	" " " "
	Rectus Femoris	Ant. Crural	"	"	Br. Prof. Fem.
	Tensor Vag. Fem.	Supt. Gluteal	1–4 L	Op. 1 L. Sp.	Ext. Circum.
Extension.	Gluteus Max.	Sup. Gluteal S. Sc.	Above	Above	Scitaic. Glut.
	Gluteus Med.	" "	"	"	Prof. Fem.
	Gluteus Min.	" "	"	"	" "
	Biceps Fem.	" "	"	"	" "
	Semimembranosus	" "	"	"	" "
	Semiter Dinosus	" "	"	"	" "
Adduction.	Adduct. Mag.	Sup. Glut. Br.Gt.Sc.	1–4 L	Above	Ob. Gl. Int. C.
	Adduct. Long.	" "	Above	"	" " " "
	Adduct. Brev.	" "	"	"	" " " "
	Pectineus	Ant. Crural	"	"	" " " "
	Gracilis	Obturator	"	"	" " " "
Abduction.	Glut. Medius	See above	Above	Above	Gluteal.
	Glut. Minimus	" "	"	"	"
	Tens. Vag. Fem.	" "	"	"	Ext. Circum.
Rotat'n outw'd.	Pyriformis	Br. from Sacral	1–4 L	Op. 1 L. Sp.	——
	Gemelli inf. et Sup.	" " "	"	"	——
	Obturator int. et Ext.	Obst. & Br. from Sc.	1–4 L	"	——
	Quadratus Femoris	5th lumb. 1st Sc.	"	"	——
Rotat'n inw'd.	Glut. Med. (ant. bun.)	See above	——	——	——
	Glut. Min. " "	" "	——	——	——

(*f*) MOVEMENTS OF LEG AND FOOT.

FUNCTION.		MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion of Leg (crus.).		Biceps Femoris	Sup. Glut. S. Scia.	2–3 L	Op. 1 L. Sp.	Prof. Femoris
		Semimembranosis	" " " "	"	"	" "
		Semitendinosis	" " " "	"	"	" "
		Popliteus	Int. Popliteal	3–4 S	"	Pr. Fem. Post. Tb.
		Gracilis	Obt. Br. Gt. Sciat.	Abv.	"	Prof. Fem.
		Sartorius	Ant. Crural	6 L	"	Popliteal
		Gastrocnemius	Int. Popliteal	Abv.	"	Post. Tib.
Ext. of Leg (crus.).		Rectus Femoris	Ant. Crural	Abv.	Bet. 11–12.	Prof. Fem.
		Vastus Externus	" "	"	"	" "
		Vastus Internus	" "	"	"	Anast. Mag.
		Crureus	" "	"	"	Pop. Pro. Fem.
Flex. of foot.		Tibialis Anticus	Ant. Tibial	Abv.	Bet. 11–12.	Ant. Tibial
		Peroneus Tertius	" "	"	"	Peroneal
		Ext. Long. Dig.	" "	"	"	Ant. Peron.
		Ext. Prop. Hallucius	" "	"	"	Ant. Tibial
Extension of foot.		Gastrocnemius	Int. Popliteal	Abv.	Bet. 11–12.	Post. Tib.
		Soleus	" "	"	"	Peroneal
		Tibialis Post.	Post. Tibial	1–2 L	"	Post. Tib.
		Peroneus Longus	Musculo Cutan.	4–5 L	"	Peroneal
		Peroneus Brevis	" "	"	"	"
		Plantaris	Int. Popliteal	Abv.	"	"
		Flex. Long. Dig.	Post. Tibial	"	"	Post. Tib.
Lateral.	ab.	Tibialis Posticus	Post. Tibial	Abv.	Bet. 11–12.	Post. Tib.
		Peroneus Brevis	Musculo Cutan.	"	"	Peroneal
	add.	Ext. Long. Hallucius	Ant. Tibial	Abv.	Bet. 11–12.	Ant. Tibial
		Tibialis Anticus	" "	"	"	" "

In the compilation of the above table it was found that the statements of Gray, Quain and other anatomists do not agree as to the function of particular muscles. In all such cases the author has accepted the authority of *Duchenne*, whose classic work, "*Physiologie des Mouvements*," still remains without an equal.

3. **Animal Mechanics.**—Animal mechanics is the application of the laws of mechanics to animal motion. The bones are used as levers; the articular surfaces of bones usually serve as fulcrums, while the power is exerted by the muscles. In a vast majority of cases the bones represent levers of the third class—in which rapidity of motion is attained at the expense of power. In other words, the arrangement of the bone-muscle organs is such that a contraction of a muscle—moderate in extent and rate of motion—is manifested by a movement of the limb which is much in excess, as to extent and rate, of the movement of the power.

In solving problems in animal mechanics the principal factors to be considered are: (I) the relative length of the two lever-arms; (II) the relative size of the muscles involved in any movement; (III) The direction in which the power acts, and (IV) the weight to be moved.

(*a*) Problems in Animal Mechanics.—Two typical problems in animal mechanics are the following:[1]

1. Determine, in a particular case, the tension exerted upon the tendo-Achillis in supporting the weight (60 kilograms) of the subject upon the ball of the foot.

2. How much tension would there be on the biceps tendon in the subject upon your dissecting table when he holds a ten-kilo. iron ball in the most advantageous position? This is a typical problem and its solution will make the difficulties to be encountered apparent. It will also show that nothing more than an approximate solution can be attained without an extended and detailed study.

Solution.—The principal muscle involved in the required action being the biceps, the most advantageous position is the one in which that muscle exerts its power in a line perpendicular to the lever. Placing the subject's arm as nearly as possible in that position, one takes the following measurements: (I) The long arm of the lever; this would be from the center of articulation between the humerus and the ulna, to the center of the 10-ko. ball, which would be, approximately, to the distal extremities of the metacarpal bone (36 cm.). (II) The short arm of the biceps lever; this would be the distance from the center of the insertion of the biceps to the fulcrum—the center of articulation (6 cm.). (III) The short arm of the lever for the Brachialis anticus. If the Brachialis anticus were exactly parallel to the Biceps the short arm would be the distance from the insertion to the fulcrum (5 cm.), as in the biceps; but it is not parallel.

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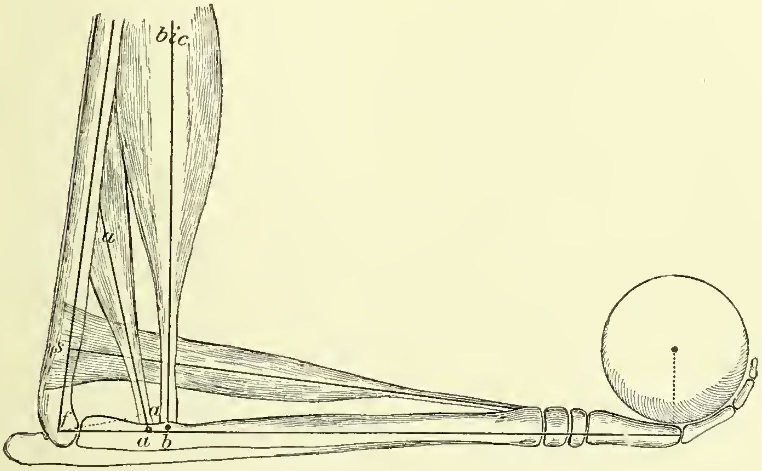
[1] Both of the problems stated above are problems in "*muscle statics.*" Such problems deal with tension upon muscles when the limb is in a certain fixed position. There are much more complicated problems which deal with the energy exerted in a more or less complex movement when the leverages and angles of tension are constantly varying. Such problems in "*muscle dynamics*" can only be solved by the application of higher mathematics. *Otto Fischer*, of Leipzig, has done much to throw light upon this field of physiology. See his "*Beiträge zur Muskel-Statik*"; also "*Beiträge zu einer Muskel-dynamik.*

FIG. 296.



Mechanics of flexion of the forearm. [The upper *a* is to be understood as *a′*.]

A line drawn from the fulcrum perpendicular to the axis of the Brach. ant., fa', is shorter than the line $f\,a$. The angle between the Brachialis anticus and the Biceps is approximately 10°; therefore the angle $a\,f\,a'$ would be approximately 10°; then $a'\,f$ is the cosine 10° or 98 per cent. of the radius $a\,f$ (5 cm.) or 4.9 cm.

(IV) The power-arm of the Supinator longus is the perpendicular distance from the fulcrum to the line of force of the Supinator longus and is represented by the line $f\,s$, which is 4.8 cm. Now the carpal and digital flexors which take origin from the humerus act as forearm flexors after having flexed the carpus and digits. In the action under consideration they would not be brought into forcible action as carpal and digital flexors. We may therefore ignore them and confine our discussion to the three muscles mentioned above.

In the action of the Biceps the long arm is 36 cm. and the short arm 6 cm.; in the action of the Brach. Ant. the long arm is 36 cm. and the short arm 4.9 cm.; in the action of the Sup. Long. the long arm is 36 cm. and the short arm 4.8 cm. Reducing these to per cent. ratios we have: For the Biceps, which we will designate as b, 16.6 per cent. leverage; for the Brach. ant., which we will designate as a, 13.6 per cent. leverage; and for the Sup. long., which we will designate as s, 13.3 per cent. leverage.

But there is another important consideration: Fick has demonstrated that when the fibers are parallel the strength of two muscles is proportional to the areas of their cross sections (*Hermann's Handbuch der Physiologie*, I., p. 295). The average ratio of the diameter of the three muscles in question is 4 : 2 : 1 respectively; but the areas of the cross sections would be proportional to the squares of the diameters or as 16 : 4 : 1, respectively. This means that with the same leverage the Biceps would lift four times as much as the Brachialis anticus and that the Brachialis anticus would, with the same leverage, lift four times as much as the Supinator longus.

We have now discussed the relation of these three factors as to *leverage* and as to *relative power* exerted.

As to leverage one may say: The power of the three muscles varies in proportion to biceps leverage (bl); brachialis anticus leverage (al); supinator longus leverage (sl) respectively, or mathematically expressed, P varies as $bl : al : sl$ or varies as $16.6 : 13.6 : 13.3$. As to cross section one may say: The power varies in proportion to the respective cross sections (s) or P varies as $bs : as : ss = 16 : 4 : 1$. Now when any function varies with two or more variable factors, its variation when influenced by the action of all of these factors at once would be represented by the product of the several variables. Then the power varies as the leverage times the cross section of each of the muscles when all act together, or expressed mathematically, P varies as $b(l\times s) : a(l\times s) : s(l\times s)$.

$b(l\times s) = 16.6\times 16 = 265.6$ or 79.7 % of the total power exerted; $a(l\times s) = 13.6\times 4 = 54.4$ or 16.3 % of the total power exerted; $s(l\times s) = 13.3\times 1 = 13.3$ or 4.0 % of the total power exerted; total $= 333.3$ or 100.0 %.

But the weight supported by the action of these muscles is 10 kilos. If the biceps does 79.7 % of the total work, it would support 7.97 kilos. What would be tension upon the tendon of the biceps when it is supporting 7.97 kilos. at the end of its lever? One needs only to use the 16.6 % leverage (7.97 ÷ 16.6 %) to find that the tension would be 47.8 kilos. A similar process shows that the approximate tension upon the tendon of the Brachialis anticus is 12 kilos. and upon the tendon of the Supinator longus 3 kilos.

(*b*) The Amount of Contraction of a Muscle bears a fairly constant ratio to the resting-length of the muscle. This law of muscle physiology was discovered and demonstrated by Ed. Fr. Weber (*"Mechanik der menschlichen Gehwerkzeuge"* 1851) and was cited by Strasser (*" Funktionellen Anpassung der Quergestreiften Muskeln*, 1883) as an example of the adaptation of muscle-tissue to the mechanical requirements of the body. Weber showed that the maximum contraction of which a muscle fiber is capable is approximately 47 % of its resting-length. Both Weber and Strasser looked upon this as the factor which determines the length of the muscles, and the location of their points of origin and insertion. In all of the skeletal muscles the tension of the contracting muscle is greater than the weight lifted. The farther the insertion of a muscle from a joint (fulcrum) the less the tension upon the muscle and the greater the amount of contraction or shortening necessary; but the inherent structure of striated muscle-tissue seems to set 47 % as the limit of the extent of its contraction. The fact that all skeletal muscles actually do contract that much (varying, however, in special instances from 44 % to 62 %) indicates that the position of the origin and insertion or the length of muscle-tissue (excluding tendon) between the origin and insertion; or, more likely, that both of *these structural features have been determined by the laws of selection and now represent in all highly organized animals the most perfect mechanical adjustment consistent with the inherent properties of muscle tissue.*

(*c*) PROBLEMS IN HUMAN LOCOMOTION.—(*a*) *The muscles used in locomotion.* Let a person stand erect with heels together; let him take several steps forward and stop in a position similar to the one which he had at the beginning. What is the mechanism of *starting?* What muscles are involved in starting? What is the mechanism of *locomotion?* What muscles are involved in locomotion? What is the mechanism of equilibration while walking? What muscles are involved in maintaining the equilibrium while walking? What is the mechanism of *stopping?* What muscles are involved in stopping? How is the equilibrium maintained during the process of stopping? What muscles are involved in the maintenance of equilibrium while standing? How does running differ from walking in respect to the *starting*, the *locomotion*, the *equilibration* and the *stopping?*

(*β*) *The energy involved in locomotion.* How far is the body lifted at each step when one walks over a level surface? When one walks up an incline of 30 degrees? When one walks down an incline of 30 degrees? Does one do work while walking down hill? If so, how may it be computed? If not, why does one become fatigued in descending an incline? How much energy will a 70-kilo. man expend in walking 1 kilo. on a level road? (Suppose the man to be 172 cm. in height, and to have a pubic height of 88 cm.) A part of the energy will be expended : (I) in lifting the body ; (II) a part, in maintaining equilibrium ; (III) a part in overcoming resistance. Express in *kilogram-meters* the amount in (I). How could (II) be determined?

C. SPECIAL MUSCULAR ORGANS: THE LARYNX.

1. SUMMARY OF THE ANATOMY.

From the standpoint of the physiologist, the following anatomical facts are important :

a. The Skeleton of the Larynx.

The skeletal foundation of the larynx consists of nine cartilages, of which five are physiologically important :

1. **The Thyroid Cartilage.**—This is the largest, and it gives to the larynx its specific shape. The prominent anterior aspect of this cartilage may be felt in the throat. The flattened sides make it evident that a cross section of the larynx would reveal for the thyroid a triangular outline, with apex forward. The posterior segment is absent.

2. **The Cricoid Cartilage.**—This is a complete ring fitted inside and below the thyroid, to whose inferior cornea it is articulated laterally. The anterior aspect of the cricoid is narrow while the posterior aspect is wide, coming well up into the thyroid space.

3. **The Arytenoid Cartilages.**—These cartilages are attached to the upper posterior margin of the cricoid cartilage. The general outline of one of these cartilages is approximately triangular, and the articulation is such as to allow the cartilages to rotate around an axis parallel to the axis of the larynx, moving in a plane at right angles to the axis of the larynx. When the arytenoids are in a position of rest, one side coincides approximately with the antero-posterior line of the larynx. The anterior angle serves for the attachment of the vocal cords and is called the *Processus vocalis.*

The axis of rotation of the two arytenoid cartilages is displaceable.

4. **The Epiglottis.**—This is a thin spatulate cartilage, above the anterior superior margin of the thyroid ; its principal function seems to be the protection of the larynx during deglutition.

b. The Muscles of the Larynx.

There are five muscles, or pairs of muscles which are important to the physiologist.

1. **The Transverse Arytenoid Muscle.**—This passes from one arytenoid cartilage to the other. Its contraction tends to draw these bodies toward the median line. (See Fig. 297, *A.*)

2. **The Posterior Crico-arytenoids.**—Each of these two muscles has its origin on the cricoid cartilage. After passing upward and outward each is inserted into an arytenoid cartilage. Contraction of these muscles tends to rotate the arytenoid cartilages upon their axis, so that *the processus vocalis is abducted.* (See Fig. 297, *P.C.A.*)

3. **The Lateral Crico-arytenoids.**—The origin is on the inner lateral aspect of the cricoid cartilage. Passing upward and backward, each is inserted into the outer aspect of the corresponding arytenoid. Contraction of these muscles tends *to adduct the processus vocalis.* (See Fig. 297, *L.C.A.*)

4. **The Thyro-arytenoid Muscles** arise from the inner anterior aspect of the thyroid and pass directly back in the plane of the vocal cords to be inserted into the outer anterior side of the arytenoids. Contraction of the thyro-arytenoids alone would adduct. This pair of muscles is involved especially in *the "fixing" of the arytenoid cartilages.*

5. **The Crico-thyroid Muscles** arise on the lower posterior part of the thyroid cartilage, externally, and pass downward and forward to be inserted into the cricoid cartilage. Contraction of these muscles lifts the anterior segment of the cricoid cartilage, or at least draws the anterior segments of the thyroid and cricoid cartilages nearer together. The result of this is to carry the upper posterior margin of the cricoid cartilage farther away from the upper anterior part of the thyroid cartilage. In other words, *to increase the distance between the two points of attachment of the vocal cords.* In other words, they are *tensors of the cords.*

c. The Innervation of the Larynx.

(*a*) The Sensory Nerve of the larynx is the *superior laryngeal* branch of the vagus.

(*b*) The Motor Innervation is through the *inferior laryngeal* for all the muscles except the Crico-thyroid, *i. e.*, the tensors of the cords. These muscles are innervated by the superior laryngeal. From this it is clear that with loss of sensation of the larynx there is loss of proper phonation.

2. THE MECHANICS OF THE LARYNX.

In the diagrammatic representation of the larynx as seen from above, *i. e.*, in line of its axis, note especially the following features :

T.C. = Thyroid cartilage.
S.C.T.C. = Superior cornu of the thyroid cartilage.
C.C. = Cricoid cartilage, posterior-superior aspect.
A.C. = Arytenoid cartilage.

x. = Axis of articulation of an arytenoid cartilage.
T.A. = Thyro-arytenoideus muscle.
a. = Arytenoideus muscle.
P.C.A. = Post. Crico-arytenoideus.
L.C.A. = Lateral Crico-arytenoideus muscle.

V.C. *The vocal cords* are attached anteriorly to the inner surface of the upper anterior segment of the thyroid cartilage and posteriorly to the processus vocalis of the two arytenoid cartilages, respectively.

Fig. 297.

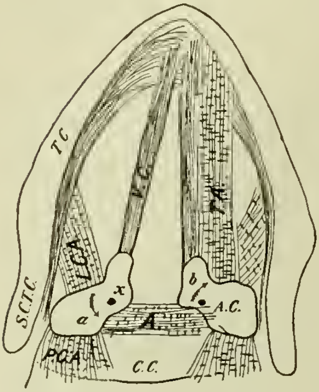


Diagram of muscles of larynx.

From the figure given it would seem that the Arytenoideus and Posterior Crico-arytenoidei would act together in rotating the arytenoid cartilage about the axis *x* in the direction of the arrow *a*. Also that the thyro-arytenoidei and the lateral crico-arytenoidei would act together in the reversed rotation as indicated by the arrow *b*; furthermore, that the first action would tend to separate the vocal cords, while the second would approximate them.

But this is only a part of the truth. The axis of rotation of the arytenoid cartilages are not fixed; *they are displaceable.*

Fig. 298.

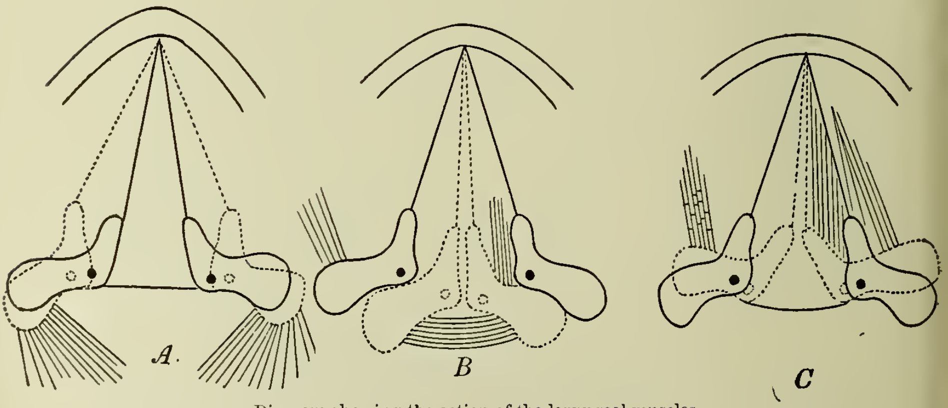


Diagram showing the action of the laryngeal muscles.

1. **The Abduction of the Glottis.**—In the three diagrammatic figures (Fig. 298, *A*, *B* and *C*) the continuous lines represent the larynx *at rest; i. e.*, in the position which the parts assume during quiet breathing. Fig. 298, *A*, shows in the dotted lines

the position produced by a contraction of the posterior crico-arytenoid muscles. The arytenoid cartilages have been rotated outward, the axes have been displaced outward, and the opening has changed from triangular to pentagonal. This position is assumed in deep inspiration. These muscles are sometimes called *abductors of the glottis*, because they separate the lateral boundaries of the glottis from the median line.

2. **The Adduction of the Glottis.**—Adduction of the lateral boundaries of the glottis may be accomplished in two ways:

(*a*) ADDUCTION BY ROTATION of the arytenoid cartilages on their axes and approximation of vocal cords alone. This is done by the *Thyro-arytenoidei* muscles acting or in conjunction with the lateral crico-arytenoidei.

(*b*) ADDUCTION BY DISPLACEMENT of the arytenoid cartilages toward the median line, by the contraction of the *Arytenoideus* muscle, supplemented by the *Thyro-arytenoidei* and the *lateral Crico-arytenoidei.* The action of the last muscles being clearly to overcome the tendency of the Arytenoideus to rotate the tips of the cartilages outward. This second form of adduction completely closes the larynx, and the groups of muscles which perform the act are often called the *Sphincters of the Larynx.*

3. **The Tension of the Vocal Cords** necessary to the production of sound is brought about by the combined action of the adductors (*b*), which simply approximate the cords, and the Cricothyroidei, whose contraction brings the ventral edges of the cricoid and thyroid cartilages nearer together, separates their dorsal aspects and thus puts the vocal cords on the stretch.

4. **The Levers of the Larynx** are levers of the first class.

3. THE ACOUSTICS OF THE LARYNX.

The larynx is a musical instrument supplied with a device for setting the air into vibration. The air thus set to vibrating is not simply the air that is being emitted from the respiratory organs, but the air which fills the air passages of the lungs. Even the tissues of the chest and head participate, to a limited extent, either as resonating or as reflecting surfaces. The rate of vibration is determined wholly by the vocal cords acting as vibrating strings. The pitch of voice depends, then, solely upon the vocal cords, while the timbre or quality depends upon the size of the chest and the size and space relations of those parts of the respiratory passages, including the mouth, external to the vocal cords.

How does the pitch of the voice vary? We have only to apply the laws of the transverse vibrations of strings to the solution of the problem. If we let l equal the length of the string, r its radius, d its density, t the tension with which it is stretched, and N the number of vibrations per second, we would have the following formula (for derivation see *Physiological Acoustics*):

$$(1) \qquad N = \frac{1}{2rl} \times \sqrt{\frac{t}{\pi d}}$$

Now π and 2 may be discarded when we express it as a variable, so we would have:

$$(2) \qquad N \text{ varies as } \frac{1}{rl}\sqrt{\frac{t}{d}}$$

We see, then, that the number of vibrations per second, *i. e.*, the pitch of the voice, depends upon four variables, and we may express them separately thus:

(I) N varies as $\frac{1}{r}$; (II) N varies as $\frac{1}{l}$;

(III) N varies as $\sqrt{t}$; (IV) N varies as $\sqrt{\frac{1}{d}}$.

These laws apply to the human voice in the following manner:

(*a*) *The pitch varies inversely as the radius of the vocal cord*, $\left(N \text{ varies as } \frac{1}{r}\right)$, but the radius of the vocal cord varies with (I) *age*, becoming thicker with advancing age; (II) with *sex*, being thinner in females than in males; (III) besides these general variations of pitch which depend upon age and sex there are *individual differences* which lead to difference of pitch in two persons of the same age and sex.

(β) *The pitch varies inversely as the length*, $\left(N \text{ varies as } \frac{1}{l}\right)$;

The length of the vocal cords vary with (I) *age*, for they take a part in the general body growth. They vary also (II) with *sex*, reaching in the average man a length of 15 mm., while in women they are but 11 mm. in average length.

(γ) *The pitch varies as the square-root of the tension*, (N varies as $\sqrt{t}$). The tension varies solely with the muscular activity of the muscles of phonation. (See above.)

It may be interesting to note here that in raising the pitch of the voice voluntarily from any chosen key-note to its fifth, whose number of vibrations would represent the ratio $\frac{3}{2}$ when compared with the key-note, it would require a tension of $\frac{9}{4}$, the original tension, or $2\frac{1}{4}$ times the original tension to produce $1\frac{1}{2}$ times the original number of vibrations per second, or to raise the pitch from *do* to *sol*. From this it is evident that the production of high notes must be a severe physical tax upon the muscles of phonation.

(δ) *Pitch varies inversely as the square root of the density,* $\left(N \text{ varies as } \sqrt{\frac{1}{d}}\right)$. But in the human vocal cords there is no essential variation in the density of the vocal cords with age, sex or other variable factors so that this law does not apply to the larynx though it does to other musical instruments.

4. THE VOICE: PHONATION.

Man possesses the function of phonation in its highest form. All animals which possess a voice are able to use it in expressing, to their associates, the various emotions and passions which move the animal mind. In most of the higher mammals phonation takes on two forms: (I) articulate phonation, in which the voice comes in short vowel tones with consonants marking the beginning of the tone (the dog's "bow-wow," the cat's "meaow," the cow's "mōō"). These are all *words;* they are used to express the passions, the emotions, or the desires of the animals. Man possesses a series of these monosyllabic race words which take the form of exclamatory, grunts, cries, shrieks, cooings, guffaws, etc., through which every passion of the human soul is instantly made known to every member of the genus *Homo* within range of the voice. Most races have developed articulate phonation into a complicated succession of articulated sounds called *speech* through the agency of which various shades of meaning may be communicated to one's associates, and a sustained and continuous succession of ideas be communicated to the hearers. (II) Unarticulated continuous phonation or song, used primarily in the expression of the more pleasurable emotions, also of pathos.

a. Speech.

The highest form of articulate phonation is called speech. The simplest existence of a member of civilized society requires of an individual a vocabulary of 300 to 500 words in the expression of his thoughts,—emotions, desires, etc. Some individuals use in the course of a year many thousand different words in the expression of their thoughts. The full vocabulary is no greater tax upon the vocal apparatus than is the scanty one because no one language possesses more than 30 to 50 different elementary sounds; and words represent various combinations of these elementary sounds. Elementary sounds are made: (I) either with open organs of articulation, and modified in *quality* by various positions of the resonating surfaces, *vowels;* (II) or with the articulating organs: lips, tongue, teeth and palate obstructing, more or less, the passage of the sound or breath, *consonants.* In one sense speech consists of a series of vowel sounds separated from each other (articulated) or *joined to each other* by a series of consonants.

The Vowels of the English language are a, e, i, o, u. König gives the fundamental vowel positions of the modifying organs as resulting in the five vowel sounds : ōō, ō, ä, ā, ē. All other English vowel sounds are formed of combinations or modifications of these fundamental tones. The English ī (long i) is a combination of ä, ē, the English ū (long u) is a combination of ē, ōō. Important modifications are made by changes in the quantity of the vowel sound. The English language has at least seventeen recognized vowel sounds.

The Consonants of the language may be classified on the basis of their acoustic qualities as *liquids* or semi-vowels : m, n, l, r, s, w, y[1] ; and mutes, including all the remaining consonants. On the basis of the mechanism of formation consonants may be classified as : (I) *explosives*, as b, p, d, t, k, g ; (II) *aspirates*, as f, v, w, s, th(in), l, sh, ch, h ; (III) *vibratives*, as r ; (IV) *resonants*, as m, n, ng. Brücke gives the fundamental consonant positions as follows : (I) articulated between the lips, *labials ;* (II) articulated between tongue and hard palate, *palato-lingual ;* (III) articulated between tongue and back portion of hard palate or the soft palate ; (IV) articulated between the two vocal cords.

The following table of consonants embodies the ideas of Brücke in a form somewhat better adapted to the English consonant sounds.

PLACE OF ARTICULATION.	ORAL.				NASAL.
	Momentary.		Continuous.		Continuous
	Aspirates.	Vocals.	Aspirates.	Vocals.	Vocals.
Labials.	p	b	——	w	m
Labio-dentals.	——	——	f	v	——
Linguo-dentals.	——	——	th(in)	th(e)	——
Palato-linguals :					
Anterior position.	t	d	s	z, l	n
Middle position.	ch	j	sh	zh, r	——
Posterior position.	k	g	——	y	ng

The relation of speech to the central nervous system is discussed at length under the physiology of the brain (q. v.).

b. Song.

The musical scale is discussed under *Physiological Acoustics* (q. v.). Though the human ear is able to appreciate a range of musical tones from a vibration rate of 16 per second up to 16,700 or 33,408 per second ; *i. e.*, a range of ten or eleven octaves ; the human voice is able to cover a range of (possesses a compass of) *two octaves*, in rather rare cases of three octaves. The two-octave range of the male voice is below that of the female voice. The reason for this is discussed above.

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[1] y sometimes replaces i as a pure vowel.

DIVISION *C.*

CHAPTER XIII.

REPRODUCTION.

THE PHYSIOLOGY AND MORPHOLOGY OF REPRODUCTION.

1. THE OVUM.
2. MATURATION.
3. FERTILIZATION.
4. SEGMENTATION.
5. THE EMBRYO: HISTOGENESIS.
   - *a.* The Development of the Germ-layers.
   - *b.* The Development of the Primitive Segments.
   - *c.* The Beginning of the Nervous System.
   - *d.* The Mesenchyme.
   - *e.* The Origin of the Urinary System.
   - *f.* Summary of Early Development: Histogenesis.
6. THE FŒTUS: ORGANOGENESIS.
   - *a.* The Circulatory System.
   - *b.* The Respiratory System.
   - *c.* The Digestive System.
   - *d.* The Uro-Genital System.
   - *e.* The Central Nervous System.
7. THE FŒTAL ENVELOPES.
   - *a.* The Fœtal Membranes.
   - *b.* Maternal Portion of Envelopes: Deciduæ and Placenta.
8. THE PHYSIOLOGY OF THE EMBRYO AND FŒTUS.
   - *a.* Nutrition.
   - *b.* Moto-Sensory Activity.
9. THE PHYSIOLOGY OF MATERNITY.
   - *a.* Pregnancy and Parturition.
   - *b.* Lactation.

REPRODUCTION.[1]

The parental phases of reproduction include all of those activities involved in the production of offspring. Two general phases in the production of offspring are (I) the transmission of hereditary characters and (II) the nourishment and protection of the young during a longer or shorter period of development.

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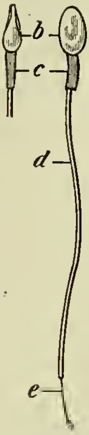
[1] The introduction to the processes of reproduction may be found in Part One—Cellular Biology. It is proposed to give here a very brief summary of mammalian reproduction and development, especially emphasizing the physiological phases of the processes.

In mammalian reproduction one may profitably consider the following special processes: (I) The *formation* of the germ cells; the *maturation* of the germ cells; the conjugation or fusion of the germ cells (*fertilization*); (II) the *segmentation* of the fertilized ovum; the *intra-uterine development* successively, of the blastoderm, the gastrula, the three-layered embryo, and the fœtus; parturition; lactation; *extra-uterine* development.

FIG. 299.



Human spermatozoa. $\frac{1000}{1}$. 1, in profile; 2, viewed on the flat; *b*, head; *c*, middle-piece; *d*, tail; *e*, end-piece of the tail, which is described as a distinct part by Retzius. (SCHAEFER after RETZIUS.)

Some of these processes represent activities of the parents; some, those of the developing young.

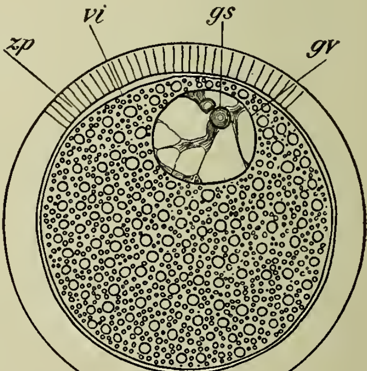
The paternal portion of the general process consists in the production of the male germ cells and assisting in the nourishment and protection of the young during its extra-uterine development. The male reproductive cell,—the spermatozoön, (Fig. 299)—serves the double purpose: (I) Of transmitting to the offspring the hereditary characters of the paternal ancestral line; and (II) of inducing in the ovum the process of segmentation.

The maternal portion of the general process consists in the production of the female germ cells and the protection and nourishment of the young during intra-uterine development and infancy, and assisting in its nourishment and protection during childhood and youth.

The offspring is passive as an individual during intra-uterine life, but its cells and tissues are exceedingly active. The activity takes the form of the following processes: Segmentation, formation of embryonic layers, development of tissues and organs drawing sustenance for these structures from the maternal organism.

Without further following the distinction between parental and embryonic processes we may now summarize the whole process of reproduction and development.

FIG. 300.



Semi-diagrammatic representation of a mammalian ovum. (Highly magnified.) *zp*, zona pellucida; *vi*, vitellus; *gv*, germinal vesicle; *gs*, germinal spot. (SCHAEFER.)

1. THE OVUM.

The ovum is a simple, single cell. The parts of this gigantic cell have received special names: the cell-wall is called the *vitelline* *membrane*; the protoplasm, with its reserve nutriment is called the *yolk*, the nucleus becomes the *germinal vesicle*; the nucleolus the *germinal dot*. (Fig. 300.)

2. MATURATION.

Before the egg is ready to be fertilized the process of maturation takes place in the following manner, in the egg of an echinoderm: (Fig. 301, *a* to *g*.)

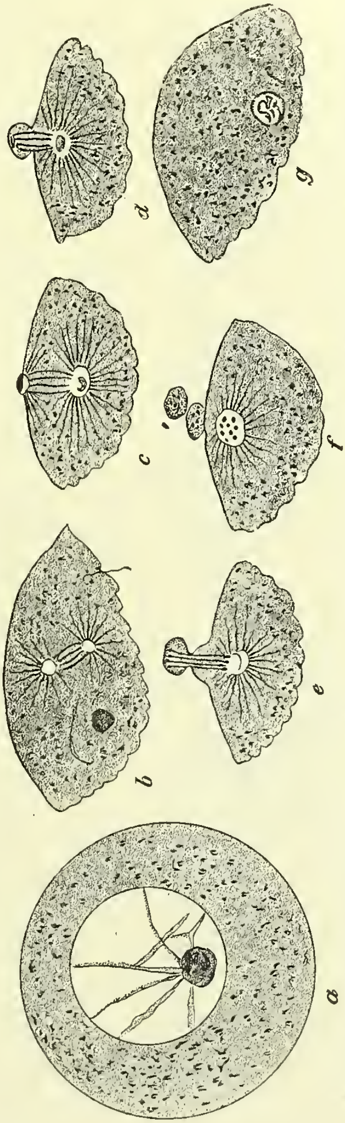
(I) The germinative vesicle gradually moves from the center of the egg towards its surface, its nuclear membrane disappears and the germinative dot breaks up into small hardly visible fragments.

(II) There arises out of a part of the nuclear substance of the germinative vesicle a *nuclear spindle* which pursues still further the direction taken by the germinative vesicle until it touches with its apex the surface of the yolk, where it assumes a position with its long axis in the direction of a radius of the sphere.

(III) A genuine process of cell-division soon takes place here, which is to be distinguished from the ordinary cell-division only in this that the two products *of cell-division are* of very unequal size.

More exactly expressed this process is a cell-budding (gemmation). This process of gemmation occurs twice. The two small cells are called polar bodies.

Fig. 301.



Maturation of egg of *Asterias gracilis*. *a*, ovarian egg; *b* and *c*, stages (I) and (II) of maturation; *d* and *e*, stage (III) of maturation; *f* shows polar bodies divided off from the ovum; *g*, mature ovum ready for fertilization; *g.f*, the female pronucleus or egg nucleus.

(IV) After the conclusion of the second process of budding the remaining part of the spindle, one-fourth of the original spindle, is left in the cortical layer of the yolk. From this arises a new, small vesicular nucleus, which consists of a homogeneous fluid substance without distinct nucleolus. From its peripheral position it usually migrates slowly back toward the middle of the egg. Thus it completes in four phases the process of maturation. There is no reason to doubt that the process of maturation in the mammalian egg is in any important feature different from that in the egg of the echinoderm.

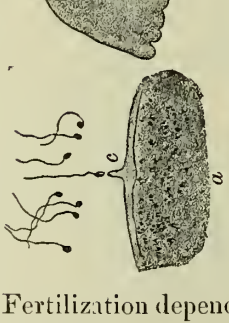


Fig. 302.

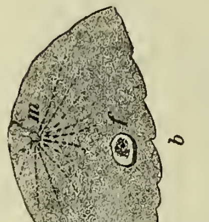


Fig. 303.

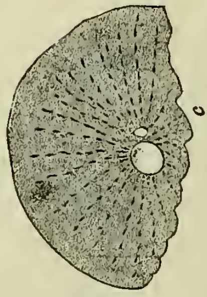


Fig. 304.

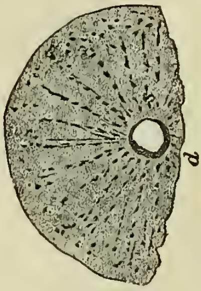


Fig. 305.

The process of fertilization in *Asterias*. *a*, the spermatozoa gathering about the attraction cone (*c*), stage (I); *b*, stage (II), showing male (*m*) and female (*f*) pronuclei; *c* and *d*, stage (III ; *ds*, the segmentation nucleus. (After Hertwig.)

3. FERTILIZATION.

Fertilization is the union of egg-cell and spermatic cell; without this union no further development of the egg is possible. The spermatic cell is the male element of reproduction ; in most animals, both vertebrate and invertebrate, the sperm cell is a flagellate cell whose head represents the nucleus and whose flagellum represents the protoplasm. The male element being the active one in reproduction the flagellum serves as a locomotory organ. (Figs. 299 and 302.)

Fertilization may take place within the body of the female or external to it, *internal* or *external fertilization*. (Internal: most vertebrates—External: fishes, amphibia and most invertebrates.)

(I) At fertilization only a single spermatozoön penetrates a sound egg, which occurs at the apex of the cone of attraction.

(II) The head of the spermatozoön is converted into the spermatic nucleus, around which the neighboring protoplasmic granules are radially arranged. (Fig. 303.)

(III) The egg-nucleus and spermatic-nucleus migrate toward each other and in most instances immediately fuse to form the *segmentation nucleus*. (Figs. 304 and 305.)

Fertilization depends on the copulation of two cell-nuclei which are derived from the male-cell and a female-cell. The male and female nuclear substances contained in the spermatic-nucleus and egg-nucleus are bearers of the peculiarities which are transmissible from parents to their offspring.

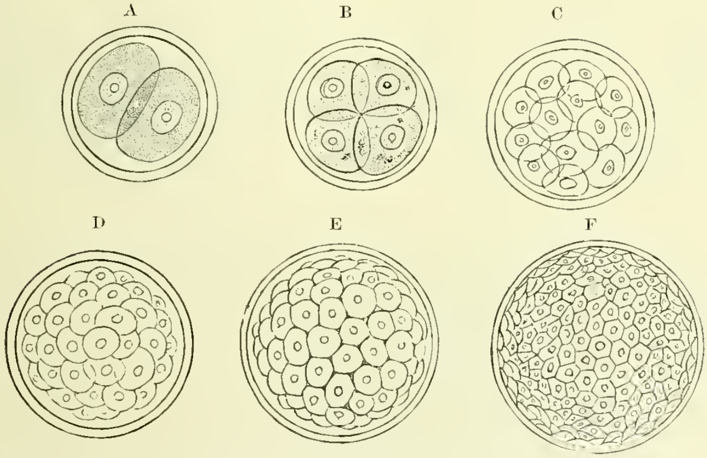
4. SEGMENTATION.

Fertilization is in most cases immediately followed by further development which begins with the division of the egg-cell into an ever increasing number of ever decreasing-sized cells—the process of *segmentation* or *cleavage*. (Fig. 306, *A* to *F*.)

(*a*) Internal Phenomena of Segmentation; 1st. *The cleavage nucleus*, at first spheroidal, forms the center of a radiation which affects the whole yolk-mass, but it soon begins to be slightly elongated, to become less and less distinct. The monocentric radiation is divided; the two newly formed radiations thereupon move to the poles of the elongated nucleus; they rapidly separate and finally each occupies a half of the egg.

The nucleus while in the process of division consists of an *acromatic* and a *chromatic* figure—the former a spindle composed of a definite number of fibers, the latter the same number of V-shaped nuclear segments—chromosomes, which lie upon the surface of the middle of the spindle. 2d. The chromosomes split lengthwise and their halves move in opposite directions, apex first, to the polar centrosomes, where they form the daughter stars, later the daughter nuclei.

Fig. 306.



Segmentation of the vitellus in the impregnated egg of the rabbit. (Dalton after Coste.)

(*b*) External Phenomena of Segmentation consist in the division of the egg-contents into cells, the number of which correspond to the number of nuclei.

5. THE EMBRYO.

Beginning with a single *cell*—the egg-cell—we have followed the development of a mass of cleavage cells—the morula, blastula, of which there are four forms.

a. The Development of the Germ-layers.

1. **The Blastula,** *with one germ-layer.*

(*a*) In Amphioxus the cleavage cavity is very large and its wall consists of a single layer of cylindrical cells of nearly uniform size. (Fig. 307, *a.*)

(*b*) In Amphibia, the cleavage cavity is small; the wall consists of a thin pole composed of small cells and a thick pole composed of several layers of large cells. (Fig. 308, *b.*)

Fig. 307.

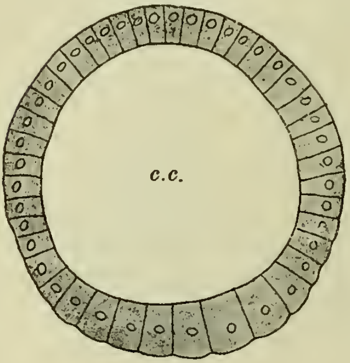


Fig. 308.

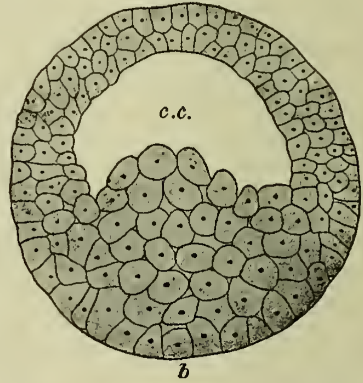
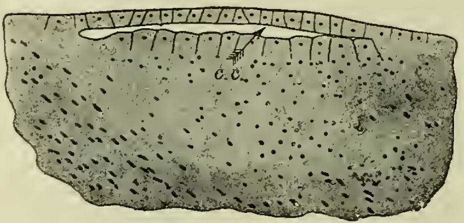


Fig. 309.



The process of blastulation. *a*, blastula of *Amphioxus*; *b*, blastula of triton (amphibian); *c*, blastula of bird; *c.c.*, cleavage cavity. (After Hertwig.)

(*c*) In Fishes, Reptiles and Birds the cleavage cavity is fissure-like or wanting; the roof is the germ-disc and the floor is the yolk mass which is not divided into cells. (Fig. 309, *c.*)

(*d*) In Mammals—Man—the cleavage cavity is spacious and filled with albuminous fluid; the wall is a single layer of hexagonal cells, with exception of one pole, whose larger cells in a mass extend into the cavity.

2. **The Gastrula.**—*With two germ-layers.* The invagination of the blastula forms the two layers of the gastrula; the outer layer is the *ectoderm* or *epiblast,* the inner layer is the *entoderm* or *hypoblast;* the cleavage cavity is obliterated; the invagination cavity is the cœlenteron, its external mouth the primitive mouth, *blastopore, primitive groove,* or *prostoma.*

(*a*) In Amphioxus the blastopore is large, the cœlenteron capacious, each germ-layer composed of single sheet of cylindrical cells. (Fig. 310.)

(*b*) IN AMPHIBIA, the blastopore is small, the mass of yolk cells is ventral to the cœlenteron, which is arched upward and is fissure-like. (Fig. 311.)

(*c*) IN FISHES, REPTILES AND BIRDS the blastopore is crescentic, the germinal disc becomes two-layered by means of ingrowth of cells from the blastopore. The cœlenteron is ventral to the lower layer of cells—*i. e.*, it is ventral to the hypoblast. (Fig. 312.)

FIG. 310.

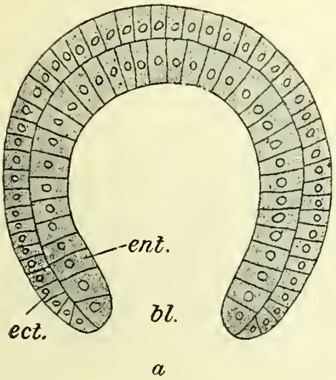


FIG. 311.

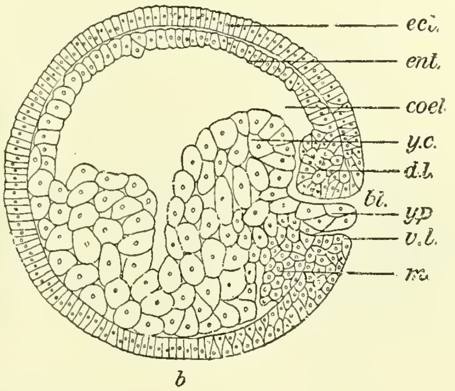
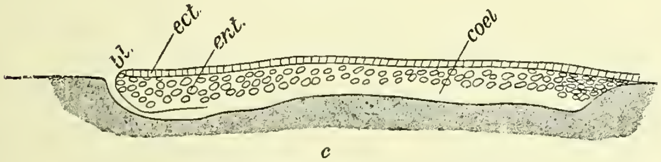
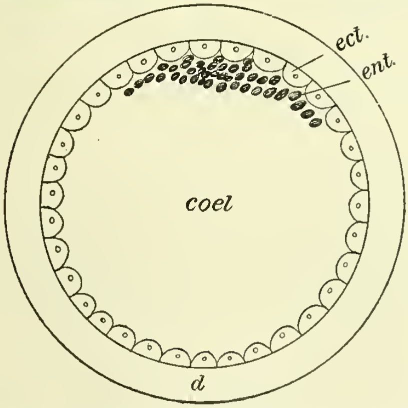


FIG. 312.





The process of gastrulation. Gastrula of amphioxus (*a*); of amphibian (*b*); of bird (*c*); of mammal (rabbit) *d*; *ect.*, ectoderm; *ent.*, entoderm; *bl.*, blastopore or primitive mouth; *coel.*, cœlenteron; *d.l.*, *v.l.*, dorsal and ventral lips; *y.c.*, *y.p.*, yolk cells and yolk plug; *m.*, mesoblast. (After HERTWIG.)

(*d*) In Mammals the blastopore is minute and circular, and over a thickened pole the cœlenteron and cleavage cavity are one and the same cavity.

In all vertebrates the gastrula presents bilateral symmetry and antero-posterior differentiation ; the blastopore is always posterior —and dorso-ventral differentiation—the yolk mass is always ventral.

3. **The Embryo** *with three germ layers.*

In all vertebrates there are formed from the roof of the cœlenteron two lateral evaginations of the inner germ-layer or hypoblast, by means of which the cœlenteron is divided into a median cavity—the intestine—and two lateral cavities, cœlomic cavities, or body cavities. The *primary* inner germ-layer thus becomes differentiated into : (I) The second inner germ-layer—hypoblast. (II) Splanchnopleure and somatopleure. (III) Notochord. These are gradually separated from each other by constrictions.

Fig. 313.

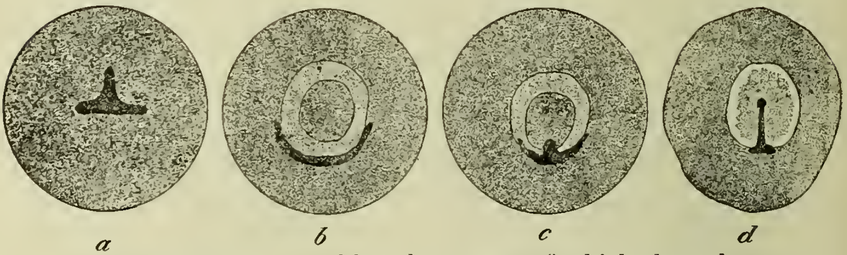
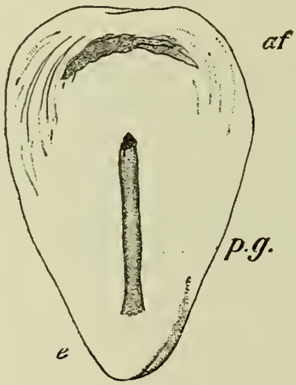


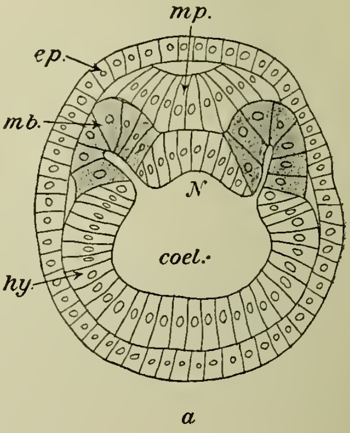
Fig. 314.



The form of the blastopore and its metamorphosis in the chick embryo. *a*, blastopore of triton ; *b* to *e*, blastopore of a chick gradually transformed from a transverse crescentic slit to a longitudinal groove—the primitive groove (*e. p.g.*). (After Hertwig.)

The development, *i. e.*, differentiation of the mesoblastic plates takes place from before backward while the growth takes place at the blastopore, thus pushing the embryonal layers forward from that

Fig. 315.



point. During the growth of the mesoblast the blastopore has been metamorphosed into the primitive groove (Figs. 313, 314). The primitive groove undergoes degeneration and is not converted into any organ in the adult.

b. The Development of the Primitive Segments.

In the mammals, birds, reptiles, amphibians and fishes, the mesoblast first appears as lateral somatic and splanchnic plates. At the time when these are constricted off from the cœlenteron the free edges fuse and immediately thicken along the dorsum either side of the notochord. This thickened plate is the *primitive segment-plate.* Immediately after formation this segment plate begins segmentation, first in the trunk (30–50) and later in the head, eleven in number (Figs. 315–319).

Fig. 316.

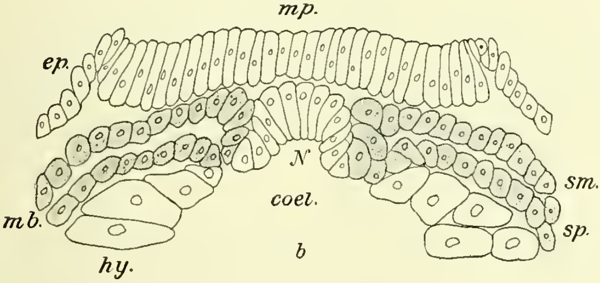
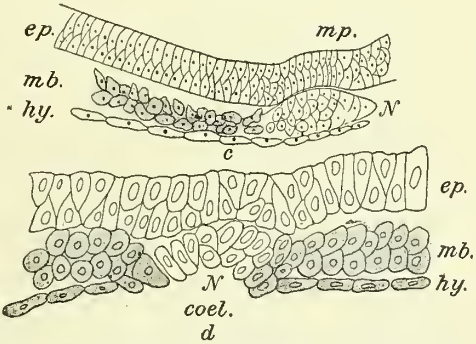


Fig. 317.

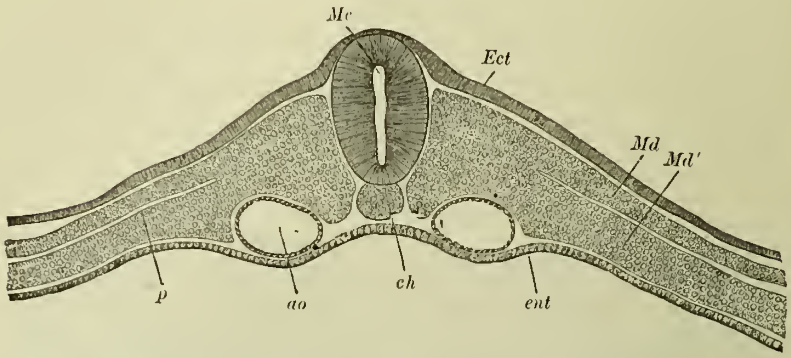


The derivation of the mesoblast and notochord from the primary inner germ layer (hypoblast). Cross section of the amphioxus (315); of an amphibian (316); of a bird (317), and of a mole (mammal) (*d*); *ep.*, epiblast; *mb.*, mesoblast; *hy.*, hypoblast; *coel.*, cœlenteron; *N*, notochord. Note that in the amphibian (*b*) the mesoblast is pretty clearly divided into somatopleure (*sm*) and splanchnopleure (*sp.*). (Hertwig after Balfour, Heape, *et al.*)

c. The Beginning of the Nervous System.

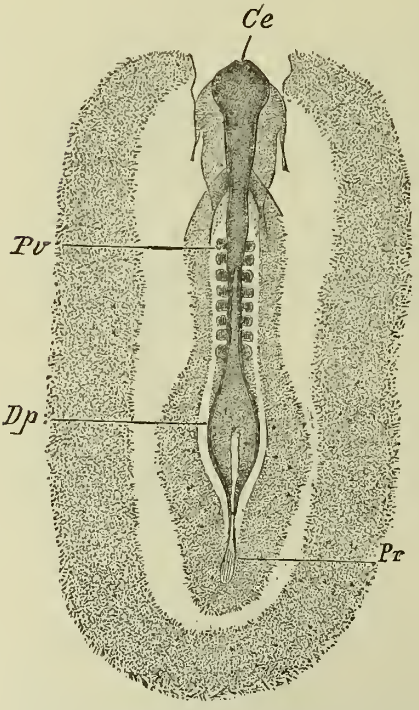
The central nervous system of vertebrates is one of the first to be established after the separation of the germ into the three primitive layers, epiblast, mesoblast and hypoblast. It is developed out of a broad band of the epiblast, the medullary plate, which lies in the median line just over the notochord. Along this band the epiblastic cells become elongated cylindrical, while the remaining epiblast is composed of flattened plates joining by their edges. An evagination of the margins of the band forms the dorsal folds or *medullary folds.* A continuation of the evagination and a coalescence of the edges of the folds accomplishes a closure of the *neural tube.* (Figs. 315–318.)

Fig. 318.



Transverse section of embryo chick, through closed portion of medullary canal. *Mc*, medullary canal; *ep*, epiblast; *Hy*, hypoblast; *Md*, *Md'*, outer and inner laminæ of mesoderm, *i. e.*, somatopleure and splanchnopleure; *p*, peritoneal space; *ch*, chorda dorsalis; *ao*, aorta; *N*, neural tube; *P.sP*, primitive segment plate. (Kölliker.)

Fig. 319.



Embryo of chick, about the fortieth hour of incubation. *Ce*, cephalic extremity; *Pv*, primitive segments or proto-vertebræ; *Dp*, dorsal plates, still widely separated in the caudal region; *Pr*, primitive groove. (Kölliker.)

The part of the neural tube which forms the brain becomes segmented early in the second day of incubation, twenty-fourth to thirtieth hour in the chick, into three primary brain-vesicles: (I) the *primary fore-brain vesicle,* (II) the *mid-brain vesicle,* (III) the *primary hind-brain vesicle.* Between the thirtieth and thirty-sixth hour of incubation the primary fore-brain vesicle gives off two lateral evaginations,—the *optic vesicles,*—and the primary hind-brain vesicle becomes divided into the *cerebellar vesicle* and the *medullar vesicle.* The closure of the neural tube or canal begins at the mid-brain and progresses anteriorly over the fore-brain and posteriorly over the cerebellar and medullar vesicles and proceeds along the spinal cord finally closing it in at the posterior end. (Fig. 318.)

Now it will be remembered that the blastopore, by virtue of the metamorphosis of the crescentic fold is now located at the anterior end of the primitive groove. The closing of the neural canal posteriorly includes the anterior end of the primitive groove with the blastopore. It thus transpires that the blastoporic canal forms a direct communication between the neural canal and the cœlenteron or alimentary canal. This connection persists some time and is known as the *neurenteric canal.* It finally becomes obliterated through fusion of its walls. Thus the last vestige of the blastopore of the higher vertebrates becomes extinct in the early stages of embryonic development.

d. **The Mesenchyme.**

Soon after the formation of the primitive segments, these, which are at first solid, soon acquire a small cavity around which the cells are arranged into a continuous epithelium. The part of the wall lying at its lower median angle begins to grow with extraordinary rapidity and to furnish a mass of embryonic connective tissue which spreads itself around the cord and neural tube (Hertwig). Out of the dorsal and lateral parts of the primitive segment arises the trunk musculature. The *mesenchyme* arises from three other places of the mesoblast besides the primitive segments, *i. e.*, from the splanchnopleure, from the somatopleure and from that wall of the primitive segment turned toward the epiblast. These four origins of the mesenchyme justify a classification of this important embryonic structure as (I) *axial mesenchyme,* (II) *splanchnic mesenchyme,* (III) *somatic mesenchyme* and (IV) *dermal mesenchyme.*

The method by which the mesenchyme arises is peculiar: (I) there is a rapid growth of the cells at some point in the mesoblast, accompanied by (II) a vigorous amœboid movement. This combination makes invagination or evagination of a body of cells a mechanical impossibility, instead of that process, *individual cells* leave the parent epithelium and, by virtue of their continued amœboid movements, wander between the somatopleure and epiblast or between the splanchnopleure and hypoblast, as the case may be. The origin and destiny of the mesenchyme have been for more than a decade a riddle whose solution has engaged the attention of His, Kölliker, Heape, Waldeyer and other embryologists.

At the time of the formation of the mesenchyme—end of first day in the chick—two necessities begin to press themselves upon the developing organisms: (I) necessity for mechanical support, and (II) necessity for nutrition. The first of these necessities urges itself upon the axial part of the embryo, for there the delicate nervous system is passing rapidly through the steps of its development. The need for nutriment will not be felt by the epiblast or by the hypoblast, for these layers are next to the supply of nourishment; but by the mesoblast, in contact with neither white nor yolk. It is a law of biology that *hungry organisms are restless* while satiated organisms are sluggish. Recall at this point the fact that the mesoblast cells which form the somatopleuric and splanchnopleuric mesenchyme *free themselves* from the mesoblast by dint of amœboid movements. These restless hungry cells are out foraging. The leucocytes of the adult body are the descendants of these restless, hungry, foraging cells of the primitive mesenchyme. How are the two necessities mentioned above satisfied?

(*a*) THE NECESSITY FOR SUPPORT for the axial nervous system is satisfied by the *axial mesenchyme* which closes about the central nervous system and the notochord, and later *develops into the axial skeleton* with *all its associated connective tissue.*

(*b*) THE NECESSITY FOR NUTRIMENT is solved by the somatopleuric and splanchnopleuric mesenchyme in the following manner, as represented by Kölliker and subscribed to by Hertwig: "At the end of the first day of incubation the masses of cells which represent the mesenchyme arrange themselves in cylindrical or irregularly limited cords which join themselves together into a close-meshed network; they are the first fundaments, both of the blood vessels and of their contents—the blood. In the spaces of the network are to be found groups of indifferent cells which afterwards become *embryonic connective tissues.*" In the beginning of the second day of incubation the "cords" acquire an internal cavity and become bounded superficially by a single layer of flattened polygonal cells—the future endothelium of the blood vessels. "The cavity of the vessel is probably formed by the penetration of fluid into the originally solid cord, thus forming the plasma of the blood by which the cells are pressed apart," some of these forming the vessel wall, some remaining floating in the fluid and becoming the leucocytes and red blood corpuscles. The red blood corpuscles originate, at the first, in the vascular area of the yolk, from yolk nuclei. They are nucleated during the early embryonic life of mammals and man and increase in numbers rapidly by division.

c. **The Origin of the Urinary System.**

Before the activities of life begin to make themselves manifest by the expenditure of energy, as in the transportation of matter through space, *e. g.*, the action of the heart walls in the circulation of the blood,—there is no need of an excretory system. If we admit then that the need for an excretory system arises during the third day in the chick, to what shall we attribute the actual appearance, during the second day, of a rudimentary urinary system? It must be attributed to HEREDITY. It is generally admitted that the genealogy of vertebrates extends through tunicates back to worms. From your studies in zoölogy you recall the segmental organs of the higher worms. A pair is located in each segment and each segmental organ is composed of: (1) a ciliated funnel, (2) a convoluted tubule, (3) a glandular segment, and (4) a muscular bladder which opens externally. But this segmental arrangement of the excretory organs is an expensive and clumsy solution of the matter. In the lower vertebrates we see the following improvements: The uriniferous tubules are segmental, but instead of opening individually on the surface of the animal, as in worms, there is a collecting tube which transfers the secretion of all the tubules of one side of the body to a posterior and ventral orifice opening near or into the cloaca. In all the higher vertebrates, including man, the *primitive kidney* or *pronephros is a segmental organ*, and is quite rudimentary, never performing the function of excretion, even in the embryo. "THE PRONEPHROS of the chick is located between the 7th and 11th somites. The pronephric duct, at its first appearance, is a short canal-like perforation of the wall of the body, which begins in the body cavity with one or several ostia and opens out upon the skin with but a single external orifice. Originally the outer and inner openings lie near together; later they move so far apart that the outer opening of the canal united with the hind-gut." (Hertwig.)

f. Summary of Early Development.

If the student has observed carefully the character of the developmental changes he has noted three phases of development going on at the same time: (I) The tendency to *unequal growth*, manifested at particular places and occurring at particular times resulting in the general morphological unfolding; (II) the histological differentiation manifesting itself in the development of new tissues (histogenesis); (III) the physiological division of labor, manifested by the general division of the functions into those of *external relations* and those of *internal relations*; and by the beginning development of various systems of organs: Nervous system, circulatory system, excretory system, etc.

(*a*) THE PRINCIPLE OF UNEQUAL GROWTH is manifested in the chick during its first two days of development by: (I) The *invagination* of the blastopore; (II) The *evagination* of the medullary folds; (III) the evagination of the three primary brain vesicles from the anterior end of the neural tube; (IV) the subsequent evagination of the optic vesicles from the fore-brain vesicle; (V) The evagination of the lateral folds of mesoblast from the median hypoblast; (VI) the *separation* of the muscle plates and their subsequent segmentation; (VII) the general emigration, from the mesoblast, of the elements of the mesenchyme; (VIII) the invagination of the pronephric canals.

(*b*) THE PRINCIPLE OF HISTOLOGICAL DIFFERENTIATION is manifested in histogenesis:

- HISTOGENESIS. Origin of Tissues.
  - I. ECTODERMIC TISSUES. Tissues of External Relation.
    - EPIBLAST PROPER.
      - *Cuticle and appendages, e.g.*, Hair, Nails, Sebaceous and Sweat Glands, Enamel of Teeth.
      - Epithelium of Conjunctiva and Cornea.
      - " " Nasal tract with glands.
      - " " Mouth with glands.
      - " " Anus and lower rectum.
      - " " Auditory canal.
    - NERVOUS SYSTEM. Neuroblast.
      - *Central Nervous System, i.e.*, Brain and Cranial Nerves, Spinal Cord and Spinal Nerves.
      - *Sensory Apparatus.*
        - Retina, Cryst. Lens, Taste Buds, Auditory Nerves, Olfactory nerves, Tactile Bodies.
  - II. ENTODERMIC TISSUES. Tissues of Internal Relation.
    - MESOBLAST.
      - *Primitive Segments.*
        - Voluntary muscular system.
      - *Somatopleure.*
        - Somatic Pleura and
        - " Peritoneum.
        - Epithelium of Genito-urinary tract.
      - *Splanchnopleure.*
        - Lung-pleura, pericardium.
        - Splanchnic peritoneum.
      - *Mesenchyme.*
        - CONNECTIVE TISSUES: Bone, cartilage, ligament, dentine, areolar tissue, tendon.
        - INVOLUNTARY MUSCULAR SYSTEM,
        - VASCULAR ENDOTHELIUM, BLOOD & SPLEEN.
    - HYPOBLAST.
      - Epithelium of *digestive tract* (exclusive of mouth and anus). Inclusive of Liver, Pancreas.
      - Epithelium of *respiratory tract.*
      - " " Urinary *Bladder* and *Urethra.*
      - " " Eustachian Tube and Tympanum.
      - " " Tonsils.
      - " " Thymus Body.
      - " " Thyroid Body.
    - NOTOCHORD.

6. THE FŒTUS: ORGANOGENESIS.

The terms *fœtus* and *embryo* are used synonymously by some authors, while by others they are given different significations- Gould defines fœtus as, "the embryo in later stages of development," but uses embryo and fœtus synonymously. The author, following in a general way the Am. Text-book of Obstetrics, will use the terms in the following sense: the *embryo* is the young in its early stages of development *when tissues are being developed;* the *fœtus* is the young at a later stage of development *when organs, especially systems of organs, are being given their finishing touches: i. e.,* the term embryo covers the period of histogenesis, and the term fœtus covers the period of organogenesis.

Under the caption *fœtus* we shall briefly discuss the development of the various systems of organs.

a. The Circulatory System.

1. **General Considerations.**—(*α*) *The simplest heart* among the vertebrates is a rhythmically contracting tube: the heart of the highest vertebrate is at first a rhythmically contracting tube.

(*β*) *Intermediate classes of vertebrates* have *two-* and *three-*chambered hearts, and the highest classes have the four-chambered heart: the heart of the highest vertebrate passes from the original tubular condition through the two- and three-chambered condition during fœtal development and finally after birth assumes the functionally four-chambered heart.

(*γ*) *The one- and two-chambered condition of the heart* makes it necessary for the heart contractions to propel the blood in one circuit through a double system of capillaries: (I) the capillaries of the respiratory system, and (II) the capillaries of the general circulation. The circulatory system of the highest vertebrates passes through this condition and reaches, in extra-uterine life, a condition in which one-half of the heart propels the blood through the respiratory system while the other half propels it through the general system.

(*δ*) *In the lower vertebrates* the blood passes from the heart directly into a system of branchial arches or gill-arches; the highest vertebrate possesses this system of gall-arches during the early part of its development. These arches are gradually reduced during the three- and four-chambered stages. Our aortic and pulmonary arches represent the last two pairs of arches.

(*ε*) *In the amphibia and reptiles,* classes of vertebrates which possess three-chambered hearts—the purer blood passes to the anterior part of the body; while the less pure blood passes to the posterior part of the body. In the human fœtus the functionally three-chambered heart distributes the blood in a similar way. This probably accounts, in part, for the large head and small legs of the fœtus. (Fig. 320.)

2. **Special Metamorphosis of the Heart.**—During the second day of the chick's development the heart is practically a straight tube formed by the fusion, along the median line, of a double, tubular heart-fundament; continuous posteriorly with the two

Omphalo-mesaraic veins and anteriorly with the bifurcated aorta. The endothelial partition of the heart soon disappears, leaving a single tube with somewhat thickened muscular walls. The dorsal aortæ, in the meantime, pass laterally around the alimentary canal and fuse ventrally, forming the single aortic trunk which joins the anterior end of the heart or Bulbus Arteriosus. As soon as the posterior venous junctions and the anterior arterial junction has been effected the already slowly and irregularly beating heart begins to send the elements of the blood through the system of tubes, the direction of the stream being at first determined not by valves but by virtue of a postero-anterior peristalsis.

Fig. 320.

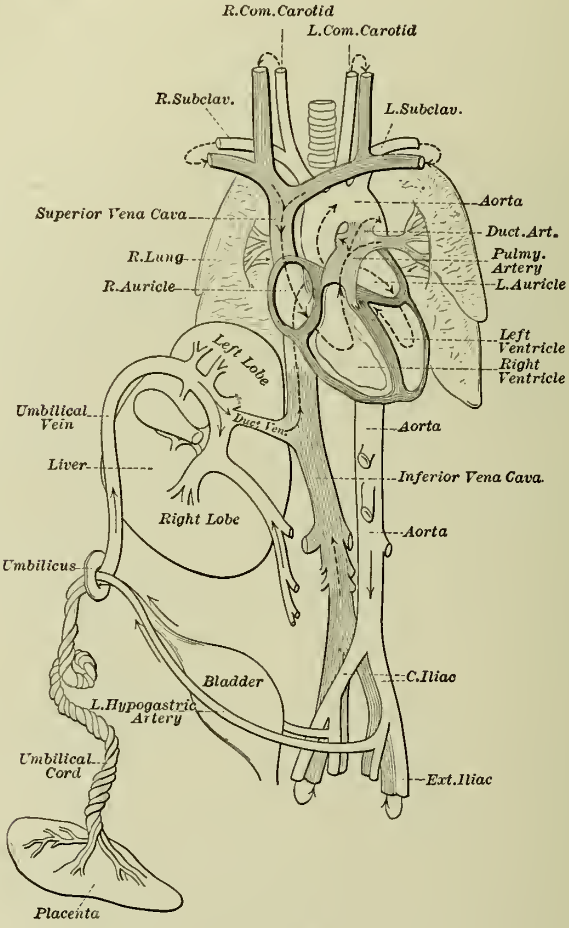
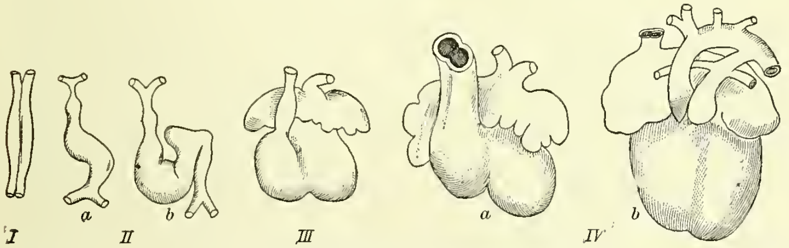


Diagram of the fœtal circulation. (Kirke.)

During the subsequent few hours the pulsations become regular and rapid, and the development of valves accompanies the gradual metamorphosis of the heart. The metamorphosis of the heart may be considered in four principal changes. (Figs. 321, 322, 323.)

	CHANGE DURING PERIOD.	CONDITION AT END OF PERIOD.	
I.	....	Straight muscular tube.	I
II.	CURVE of Heart-tube, through increase in length of Heart and no increase in length of pericardium.	Heart in S-shaped curve, with venous end in left dorsal region and arterial end in right ventral region.	II.
III.	DILATATION laterally of venous end and general DILATATION of central or ventracular segment and DILATATION of Bulbus Arteriosus.	Heart of Two Chambers, one double-lobed, single-chamber auricle dorsally and a single-chambered ventricle ventrally.	III.
IV.	DIVISION of whole Heart: 1st. Auricle into left and right. 2d. Ventricle into left and right. 3d. Bulbus Arteriosus into Aorta and Pulmonary Artery.	Heart of FOUR Chambers. Left Auricle, Left Ventricle and Aorta continuous and Right Auricle, Right Ventricle and Pulm. Art. continuous.	IV.

FIG. 321.



Development of the heart. The four principal stages being shown at *I-IV*; *a* and *b* are two phases of the same stage. (HERTWIG.)

b. The Respiratory System.

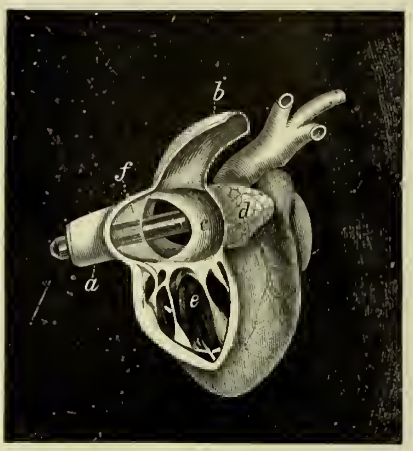
1. **General Considerations.**—(*α*) *The simplest vertebrate* respiratory system is composed of a series of gill-arches: *The highest vertebrate has gill-arches in early embryonic life.*

(*β*) *In the highest fishes* there is a combination of gills and swim-bladder which is a saccate evagination or outgrowth of the alimentary tract: *In amphibia* the gills are usually secondary in importance to the saccate lungs which are homologous to the swim-bladder: *In the highest vertebrate* the gills are rudimentary structures confined to embryonic life and never functional while the function of respiration is performed during the whole period of extra-uterine life by the lungs.

2. **Special. The Development of the Lungs.**—At the beginning of the third day in the chick, on the tenth day in the rabbit and in the human embryo when it reaches a length of about 4 mm. there arises on the ventral side of the œsophagus a groove

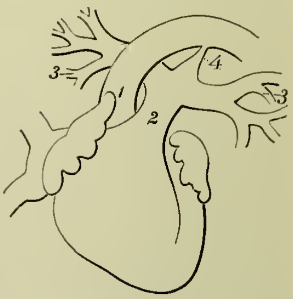
which is slightly enlarged at its anterior end. Soon the groove-like evagination becomes separated from the alimentary tube by two lateral ridges; this is the first indication of a differentiation into œsophagus and trachea. There then grow out from the enlarged posterior ends of the groove two small sacs towards the two sides of the body—the fundaments of the right and left lung.

FIG. 322.



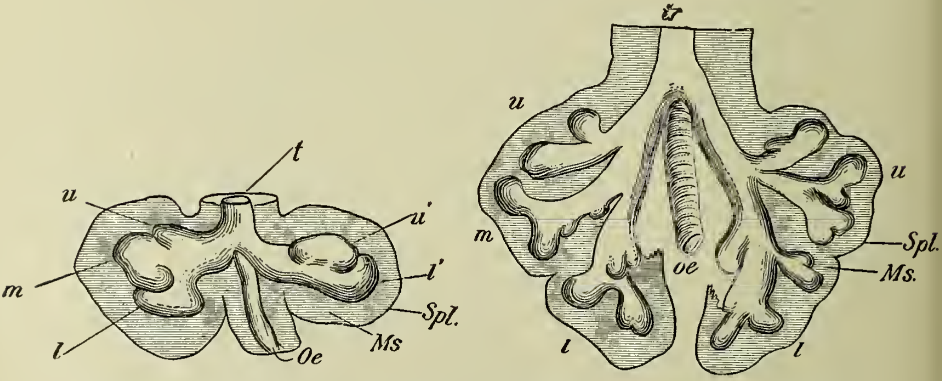
Heart of the human fœtus, at the end of the sixth month. *a*, inferior vena cava; *b*, superior vena cava; *c*, cavity of the right auricle, laid open from the front; *d*, appendix auricularis; *e*, cavity of the right ventricle; *f*, Eustachian valve. The bougie, placed in the inferior vena cava, can be seen passing behind the Eustachian valve, just below the point *f*, then crossing, behind the right auricle, through the foramen ovale, to the left side of the heart. (DALTON.)

FIG. 323.



Heart of infant, showing the disappearance of the arterial duct after birth. 1, aorta; 2, pulmonary artery; 3, 3, pulmonary branches; 4, ductus arteriosus becoming obliterated. (DALTON.)

FIG. 324.



a *b*

Early development of the lung. *t*, trachea; *Oe*, œsophagus; *u*, *m*, *l*, upper, middle and lower right lobes; *u'*, *l'*, upper and lower left lobes; *Spl.*, splanchnopleure; *Ms*, mesenchyme. (From HERTWIG after HIS.)

These lung sacs are enveloped in a thick layer of mesenchymic connective tissue which is covered externally by the thin splanchnopleure—the future lung-pleura. Two stages are recognizable in the metamorphosis of the primitive lung-sacs of man and of mammals.

(I) *The first bud-like outgrowths on the two sides of the body are not symmetrical* because the left *lung-sac produces two* and the right *lung-sac produces three bud-like enlargements* (Hertwig). These buds are the fundaments of the lobes of the lungs. From this point on the division is dichotomous. Continuous division and evagination proceed during six months in the human embryo. During this period the terminal branches are simply saccate or vesicular and are called *primitive lung vesicles.* (Fig. 324, *b.*)

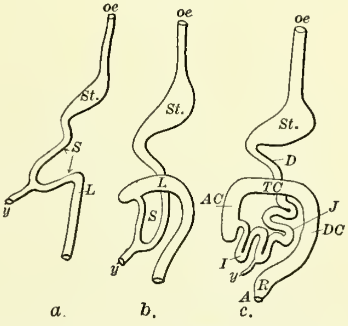
(II) During the last three months of intra-uterine life, "there arise close together on the fine terminal of the bronchial tree—on the alveolar passages and on their terminal vesicular enlargements—very numerous small evaginations—the *pulmonary alveoli*" (Kölliker). These are only $\frac{1}{3}$ to $\frac{1}{4}$ as large in the fœtus as in the adult, and the extra-uterine growth of the lung is to be attributed to their expansion rather than to their multiplication.

c. The Digestive System.

1. **General.**—(*a*) *In all vertebrates* the stomach is produced by a simple dilatation of the alimentary canal, just behind the heart in the lower vertebrates and just posterior to the diaphragm in mammalia. (Fig. 325.)

(*β*) *In all vertebrates* two glands are evaginated from the duodenum;—the *liver* is evaginated into the ventral mesentery and *pancreas* into the dorsal.

FIG. 325.



Development of the alimentary canal. *oe*, œsophagus; *St.*, stomach; *S*, small intestine; *L*. large intestine; *y*, yolk duct; *D*, duodenum; *J*, jejunum; *I*, ileum; *AD*, *TC*, *DC*, ascending, transverse and descending colon; *R*, rectum; *A*, anus.

2. **Special Development of Digestive Glands.**—(*a*) THE LIVER early becomes bilobed,—later these two primitive lobes are variously subdivided in different classes of vertebrates,—and the evaginations take the form of thick-walled tubes or "*hepatic cylinders*" which unite into a network. The small lumina of the cylinders become the bile ducts which are surrounded by the secreting parenchyma of the liver. This latter, as well as the epithelial lining of all gall ducts, is of hypoblastic origin, while the connective tissue framework and the vascular system of the liver is from the mesenchyme, the organ being encapsuled with splanchnopleure or splanchnic peritoneum.

(*b*) The Pancreas follows a general course of development quite parallel to that of the liver.

d. The Uro-Genital System.

For general considerations see above under "Origin of the Urinary System."

1. **The Indifferent Stage.**—This stage is characterized by all the organs being contained in two longitudinal uro-genital ridges, one on each side of the body and projecting from the dorsal wall into the peritoneal cavity. At the caudal end of the abdomen the two ridges draw closer together and finally come into contact with the anal region of the alimentary canal. The substance of the ridge comprises the Wolffian body of mesonephros and the genital epithelium. The ducts are two in number and are the result of longitudinal division of the original pronephric duct. The inner one of the two resulting ducts is the mesonephric or Wolffian duct and during the period when the mesonephros functions as a urine-excreting organ conducts the urine to the cloaca; this condition is permanent in fishes and amphibians. The outer one of the resulting ducts is the Müllerian duct. Now in the male *the Wolffian duct* becomes the *genital duct*, while *in the female the Müllerian duct becomes the genital duct.*

Fig. 326.

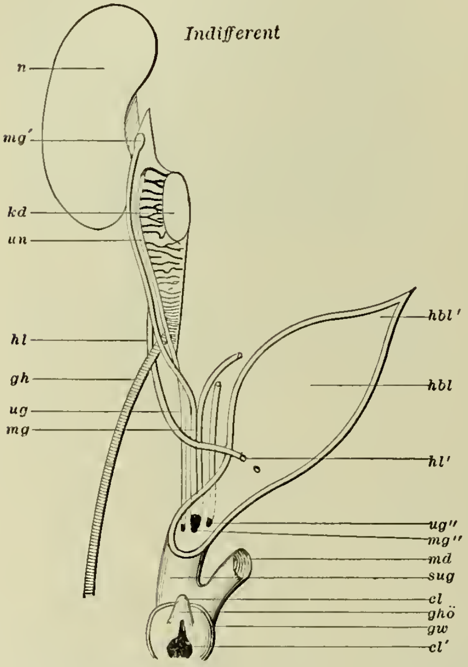


Diagram of the indifferent fundament of the uro-genital system of a mammal at an early stage. *n*, kidney; *kd*, sexual gland; *un*, primitive kidney; *ug*, mesonephric duct; *mg*, Müllerian duct; *mg'*, its anterior end; *gh*, gubernaculum Hunteri (mesonephric inguinal ligament); *hl*, ureter; *hl'*, its opening into the urinary bladder; *ug''*, *mg''*, openings of the mesonephric and Müllerian ducts into the sinus urogenitalis (*sug*); *md*, rectum; *cl*, cloaca; *ghö*, sexual eminence; *gw*, sexual ridges; *cl'*, external orifice of the cloaca; *hbl*, urinary bladder; *hbl'*, its elongation into the urachus (the future lig. vesico-umbilicale). (Hertwig.)

2. **The Differentiated Stage.**—(*a*) Changes Common to Both Sexes are: (i) The union of the caudal ends of the uro-genital ridges to form a *single median* uro-genital cord. (ii) The ducts of the *uro-genital cord* open into a cloaca with the rectum.

(III) The cloaca gradually divides into the uro-genital sinus and the anus. (IV) The allantois also opens into the cloaca and in extra-uterine life *the dilated remnant* of the *allantois becomes* the *urinary bladder*. (V) *From the lower end* of the *mesonephric* or *Wolffian duct there evaginates* the metanephric duct or *ureter*. This grows into that part of the *uro-genital ridge* which lies just posterior to the Wolffian body or mesonephros. The mass of the uro-genital ridge now lying about the dilated and divided ureter is the fundament of the metanephros or permanent kidney. While the fundament with the ureter gradually advances anteriorly, the end of the ureter differentiates into the pelvis, calyces and the collecting tubules of the pyramidal portion, and the cortical fundament gradually develops the malpighian corpuscles and the convoluted tubules. (VI) The genital epithelium in the region of the mesonephros develops into the *genital gland*, while the Wolffian body—mesonephros—lapses into functional or rudimentary appendages of that gland.

FIG. 327.

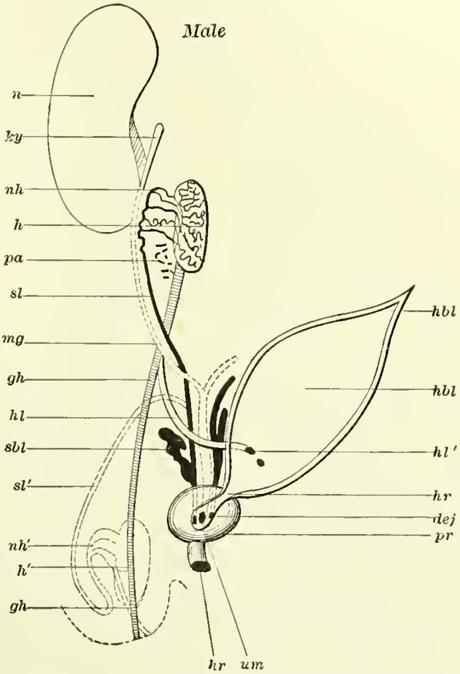


Diagram to illustrate the development of the male sexual organs of a mammal from the indifferent fundament of the uro-genital system. The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the male sexual organs take after the completion of the descensus testiculorum. *n*, kidney; *h*, testis; *nh*, epididymis; *pa*, paradidymis; *hy*, hydatid of the epididymis; *sl*, vas deferens; *mg*, degenerated Müllerian duct; *um*, uterus masculinus, remnant of the Müllerian ducts; *gh*, gubernaculum Hunteri; *hl*, ureter; *hl'*, its opening into the bladder; *sbl*, vesiculæ seminales; *hbl*, urinary bladder; *hbl'*, its upper tip, which is continuous with the ligamentum vesico-umbilicale medium (urachus); *hr*, urethra; *pr*, prostata; *dej*, external orifice of the ductus ejaculatorii. The letters *nh'*, *h'*, *sl'* indicate the position of the sexual organs after the descent has taken place. (HERTWIG.)

Fig. 328.

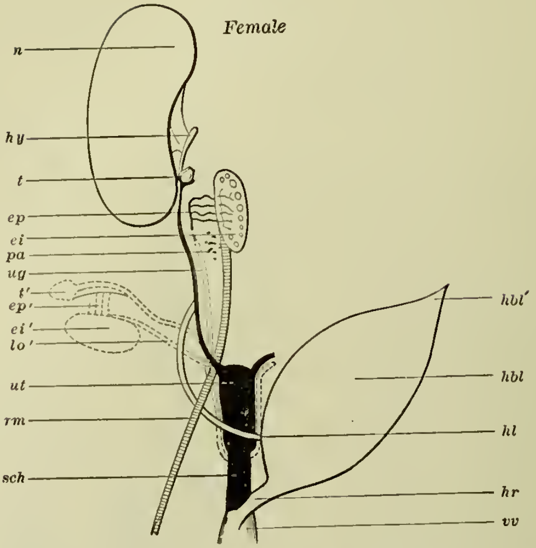


Diagram to illustrate the development of the female sexual organs of a mammal from the indifferent fundament of the uro-genital system. The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the female sexual organs take after the completion of the descensus. *n*, kidney ; *ei*, ovary ; *ep*, epoöphoron ; *pa*, paroöphoron ; *hy*, hydatid ; *t*, Fallopian tube (oviduct) ; *ug*, mesonephric duct ; *ut*, uterus ; *sch*, vagina ; *hl*, ureter ; *hbl*, urinary bladder ; *hbl'*, its upper tip, which is continuous with the ligamentum vesico-umbilicale medium ; *hr*, urethra ; *vv*, vestibulum vaginæ ; *rm*, round ligament (inguinal ligament of the primitive kidney); *lo'*, ligamentum ovarii. The letters *t'*, *ep'*, *ei'*, *lo'* indicate the positions of the organs after the descent. (Figure and description from Hertwig.)

(*b*) Sexual Differentiation. (Hertwig.) (See Figs. 326–328.)

Male Sexual Parts.	Indifferent : Common form from which both arise.	Female Sexual Parts.
Testis. Seminal Ampullæ and Tube.	Germical Epithelium.	Ovary. (Ovarian follicles.)
(*a*) Epididymus. (*b*) Paradidymus.	Mesonephros or Wolffian Body.	(*a*) Epoöphoron. (*b*) Paroöphoron (Parovarium or organ of Rosemüller).
Vas Deferens and Seminal Vesicles.	Mesonephric Duct.	
Hydatid of Epididymus. Sinus Prostaticus (Uter. masc. .	Müllerian Duct.	Uterus and Vagina. Oviduct and Fimbriæ.
Kidney.	Metanephros.	Kidney.
Ureter.	Metanephric Duct.	Ureter.
Gubernaculum Hunteri.	*Inguinal ligt. of Mesoneph.*	*Round Ligament.*
Urethra, Membranous and Prostatic Part.	Sinus Uro-genitalis.	Vestibulum Vaginæ.

c. The Central Nervous System.

1. **General Considerations.**—(*a*) *In all vertebrates* the central nervous system is developed out of the thickened region of the

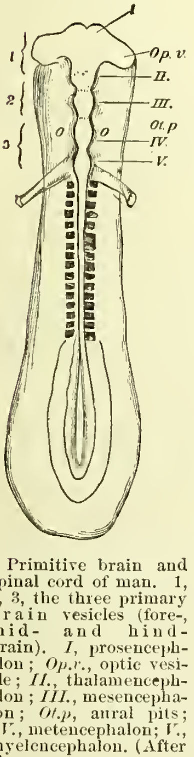
outer germ-layer which is designated as the *medullary plate.* The medullary plate is folded together to form the *neural tube.*

(β) *In the lowest vertebrates* the neural tube is not differentiated into *brain* and *spinal cord.* In the higher vertebrates there is at first no differentiation between brain and spinal cord.

(γ) *In fishes* the brain consists of five lobes not very unlike in size. An early step in the development of the brain of higher vertebrates is the formation of five lobes or vesicles.

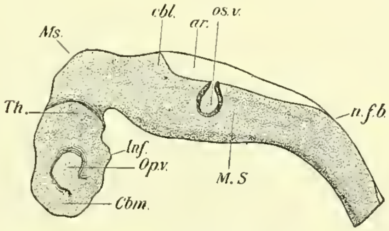
(δ) The ascending scale of vertebrates is marked by an *increasing preponderance* of the *cerebrum over* the *other segments* of the brain. The highest vertebrate in its embryonic development shows an ever increasing preponderance of the cerebrum over other parts.

FIG. 329.



Primitive brain and spinal cord of man. 1, 2, 3, the three primary brain vesicles (fore-, mid- and hind-brain). *I*, prosencephalon; *Op.v.*, optic vesicle; *II.*, thalamencephalon; *III.*, mesencephalon; *Ot.p*, aural pits; *IV.*, metencephalon; *V.*, myelencephalon. (After HAEKEL.)

FIG. 330.



A somewhat later stage of the human brain. *Cbm.*, cerebrum (prosencephalon); *Inf.*, infundibulum; *Th.*, inter-brain (thalamencephalon); *Ms.*, mid-brain (mesencephalon); *cbl.*, cerebellum (metencephalon); *ar.*, area rhomboidalis; *M.O.*, medulla oblongata (myelencephalon); *n.*, flex. nuchal flexure. (After HIS.)

2. Special: Development and Metamorphosis of the Human Brain.—(α) The part of the neural tube which forms the brain becomes segmented into the three primary *brain vesicles* mentioned above.

(β) The lateral walls of the fore-brain vesicles are evaginated to form the *Optic Vesicles* and the anterior wall to form the *secondary Fore-brain Vesicle,* the CEREBRUM or Prosencephalon.

(γ) The Hind-brain vesicle is divided by constriction into the vesicle of the CEREBELLUM—Metencephalon—and the MEDULLA—Myelencephalon.

(δ) Thus from the three primary brain vesicles there arise five secondary ones arranged in a single series, one after the other in a straight line (Fig. 329):

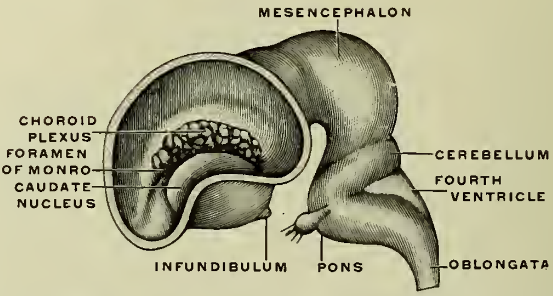
(I) Cerebrum—prosencephalon.

(II) Inter-brain—thalamencephalon—with the laterally attached optic vesicles.

(III) Mid-brain—mesencephalon.
(IV) Cerebellum—metencephalon.
(V) Medulla oblongata—myelencephalon.

(ε) The originally straight axis uniting the brain-vesicles to one another later becomes, at certain places, sharply bent: (I) The *Nuchal Flexure* is a ventral bending of the medulla, forming the *nuchal protuberance dorsally.* (II) The *Pontal Flexure* is a dorsal bending in the region of the pons varolii. (III) The *Cephalic Flexure* is a marked and persistent ventral bending of the mid-brain, resulting in the *cephalic protuberance.* The nuchal and the cephalic protuberances are obscured by subsequent development. (Fig. 331.)

Fig. 331.



Lateral view of the brain of a calf embryo of five cm. The outer wall of the hemisphere is removed, so as to give a view of the interior of the left lateral ventricle. *hs*, cut wall of hemisphere; *st*, corpus striatum; *am*, hippo-campus major (cornu ammonis); *d*, choroid plexus of lateral ventricle; *fm*, foramen of Monro; *op*, optic tract; *in*, infundibulum; *mb*, mid-brain; *cb*, cerebellum; *IV. V*, roof of fourth ventricle; *ps*, pons Varolii, close to which is the fifth nerve with Gasserian ganglion. (From HERTWIG after MIHALKOVICS.)

(ζ) In the metamorphosis of the vesicles the following processes take place: (I) Certain regions of the walls become thickened, other regions become thinner and do not develop nervous substance (roof-membranes of third and fourth ventricles); (II) The walls of the vesicles may be evaginated or invaginated; (III) Some of the vesicles greatly exceed in their growth the remaining ones (cerebrum, cerebellum). (Fig. 331.)

The four ventricles of the brain and the aqueduct of Sylvius are derived from the cavities of the vesicles.

Of the five vesicles the mid-brain undergoes the least metamorphosis.

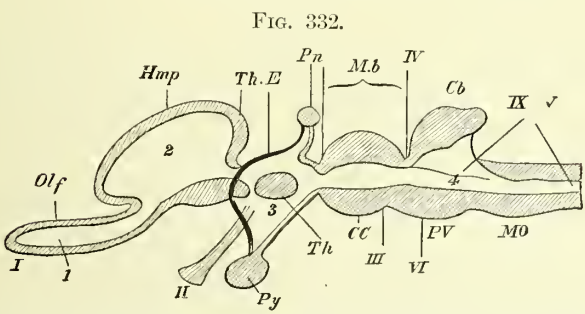
The cerebral vesicle is divided by the development of the *longitudinal fissure* and the *falx cerebri* into lateral halves, the *cerebral hemispheres.*

In man the cerebral hemispheres finally exceed in volume all the remaining parts of the brain and grow out in every direction forming a "cerebral mantle" over the other segments of the brain.

THE DEVELOPMENT OF THE BRAIN (HERTWIG). See Fig. 332.

			Floor, (f); Roof, (r); Walls, (w).	Cavity.
The Development of the Brain.	Primary Fore-brain Vesicle.	I. Fore-brain. CEREBRUM. Prosencephalon	Olfactory Lobes. (f) Cerebral Cortex. (r & w) Ant. Perf. Lamina. (f) Corpus Striatum. (f) Corpus Callosum. (r&w)	Lateral Ventricles. (1–2d Ven.).
		II. INTER-BRAIN. Optic Thalamus Thalamencephalon.	Optic Chiasm. (f) Roof-memb. of 3d V. (r) Optic Thalami. (w) Tuber Cinereum with infundibulum. (f) Corpora Albicantia. (f) Pineal Gland. (r)	Third Ventricle.
	Mid-brain Vesicle.	III. MID-BRAIN. Corpora Quadrigemina. Mesencephalon.	Post. Perf. Lamina. (f) Peduncles of Cerebrum. (f) Corpora Quadrigemina. (r) Laqueus. (w)	The Aqueduct of Sylvius.
	Primary Hind-brain Vesicle.	IV. Hind-brain. CEREBELLUM. Metencephalon.	Pons Varolii. (f) Cerebellar Cortex. (r & w) Crura Cerebelli ad Pontem. (w)	Fourth Ventricle.
		V. After-brain. MEDULLA OBL. Myelencephalon.	Medulla Oblongata. (f) Roof-memb. of 4th Ventricle. (r) Peduncles of Cerebellum. (w)	Fourth Ventricle.

FIG. 332.



Longitudinal and vertical diagrammatic section of a vertebrate brain. Lamina terminalis is represented by the strong black line joining *Pn* and *Py*. *Olf*, olfactory lobes or rhinencephalon; *Hmp*, cerebral hemispheres, mantle or prosencephalon; 3 with *II*, *Py* and *Pn*, thalamencephalon or inter-brain; *M.b*, *III*, mid-brain or mesencephalon; *Cb*, *PV*, metencephalon; 4, fourth ventricle; *MO*, medulla. (HUXLEY.)

7. THE FŒTAL ENVELOPES.

a. The Fœtal Membranes.

The term fœtal membranes may be used for that portion of the fœtal envelopes developed from the ovum. A part of the fœtal envelopes is produced by the maternal organism. If one refers to Fig. 314, *af*, he will find a crescentic dark field which represents a transverse ridge of epiblast anterior to the embryo near the anterior margin of the blastoderm. As soon as the mesoblast is formed, and divided into somatopleure and splanchnopleure, the former takes part in the formation of this fold while the latter with the hypoblast remains in close contact with the yolk. By the time that the primitive segments begin to appear the amniotic fold has taken on a horseshoe shape enclosing the head end of the embryo and sending two ridges toward the caudal end of the embryo. A cross section of the embryo at this stage will appear something like Fig. 333. The two lateral folds approach each other over the median dorsal line of the embryo and meet and fuse from before backwards, thus forming a double sac, an inner true *amnion*, composed of epiblast internally and somatopleure externally ; and an outer false amnion or *chorion*, composed of epiblast externally and somatopleure internally (see Fig. 334). The chorion presents villi over a considerable portion of the surface of the ovum. At first these villi are practically equal in development but after the allantois becomes developed, the villi in the region of that organ are rapidly increased in size, while those in other regions become obliterated. These facts are represented in Figs. 335 and 339.

Fig. 333.

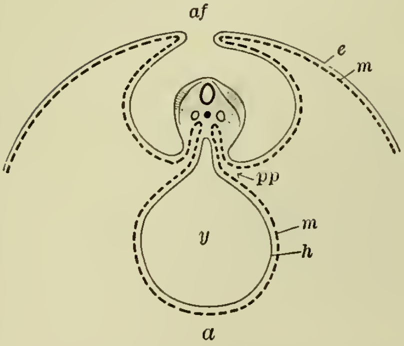
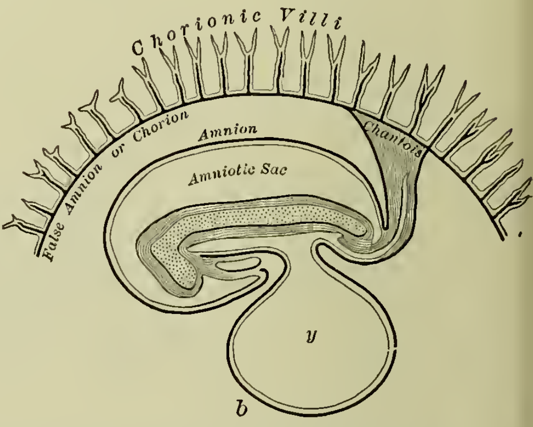


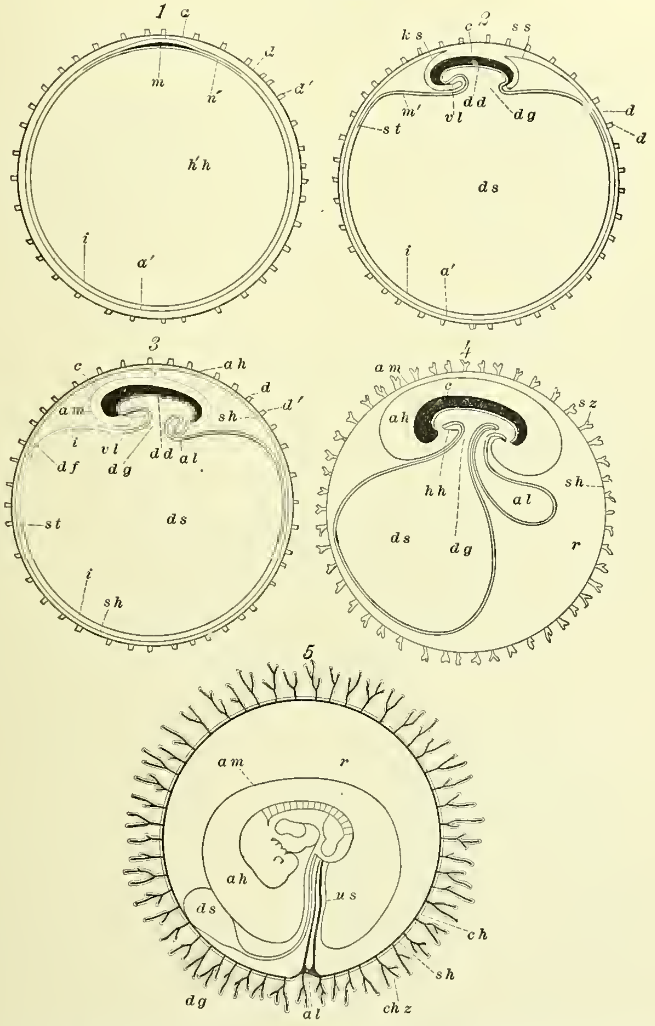
Fig. 334.



Diagrammatic figures of the development of the fœtal membranes. *af*, amniotic fold ; *e*, epiblast ; *m*, mesoblast ; *h*, hypoblast ; *pp*, pleuro-peritoneal cavity. Note that the amniotic sac is ined with epiblast, and that the chorion is lined with somatopleure, the epiblast being external, land covering the chorionic villi. (The *Allantois* is by mistake Chantois in Fig. 334.)

The *allantois* is an evagination from the ventral side of the primitive hind gut and is composed of hypoblast internally and splanchnopleure externally. While the yolk-sack (*ds*) decreases in size the allantois (*al*, Fig. 335) increases ; finally reaching the chorion where it forms the fœtal portion of the placenta. The allantois is accompanied by two umbilical arteries and an umbilical vein. These send branches into the chorionic villi of the placenta. The *umbilical cord* is composed of the arteries and vein, the shriveled yolk-stalk, the allantoic stalk, a gelatinous embryonic connective tissue and the whole enclosed in amnion. A careful study of Figs. 334 and 335 will reveal the relations of these structures much more clearly than a description could do.

Fig. 335.

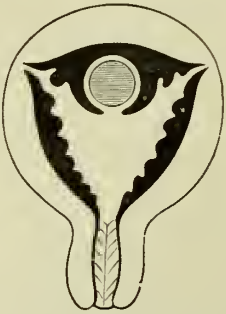


Diagrammatic figures, illustrating the development of the mammalian embryo and the fœtal membranes. 1, the blastodermic vesicle invested in the zona pellucida, and showing at its upper pole the embryonic area; 2, shows the pinching off the embryo from the yolk-sac, and the formation of the amnion; 3, further development of amnion, and commencement of allantois; 4, completion of amnion and growth of allantois. The false amnion, or subgonal membrane, gives off villous process. 5, the allantois has grown all round the vesicle, and gives off processes into the villi which are much larger than before. The yolk-sac is greatly reduced in size. *a*, epiblast of embryo; *a′*, epiblast of non-embryonic part of blastodermic vesicle; *al*, allantois; *am*, amnion; *ch*, chorion; *ch* 2, chorionic villi; *d*, zona pellucida; *d′*, processes of zona: *dd*, embryonic hypoblast; *df*, area vasculosa; *dg*, yolk-stalk; *ds*, yolk-sac; *e*, embryo; *hh*, pericardial cavity; *i*, non-embryonic hypoblast; *kh*, cavity of blastodermic vesicle; *ks*, head-fold of amnion; *m*, embryonic mesoblast; *n*, non-embryonic mesoblast; *r*, space between true and false amnion; *sh*, false amnion, or subgonal membranes; *ss*, veil-fold of amnion; *st*, sinus terminalis; *si*, processes of zona pellucida; *vl*, ventral body-wall of embryo. (Kölliker.)

b. Maternal Portion of Envelopes: Deciduæ and Placenta.

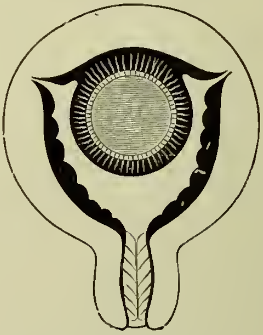
The maternal organism plays an important part in the formation of the fœtal envelopes. Figs. 336, 337, 338 show the formation of the deciduæ. Fig. 339 shows the three portions of the deciduæ; (I) *Decidua vera* lining the body of the uterus; (II) *Decidua reflexa*, reflected over the egg, (III) *Decidua serotina* where the chronic villi are developed. The relation of the maternal to the fœtal membranes is shown in Fig. 338. Fig. 339 shows similar structures somewhat less diagrammatic.

Fig. 336.



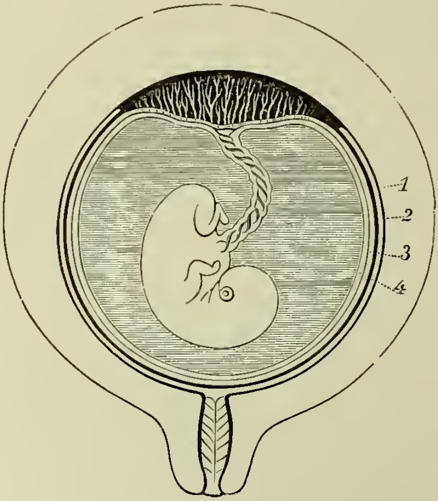
Impregnated uterus, with folds of decidua growing up around the egg. The narrow opening, where the folds approach each other, is seen over the most prominent portion of the egg. (Dalton.)

Fig. 337.



Pregnant uterus; showing the formation of the placenta by the local development of the decidua and the chorion. (Dalton.)

Fig. 338.



Pregnant human uterus and its contents, about the end of the seventh month; showing the relations of the cord, placenta and membranes.—1, Decidua vera; 2, Decidua reflexa; 3, Chorion; 4, Amnion. (Dalton.)

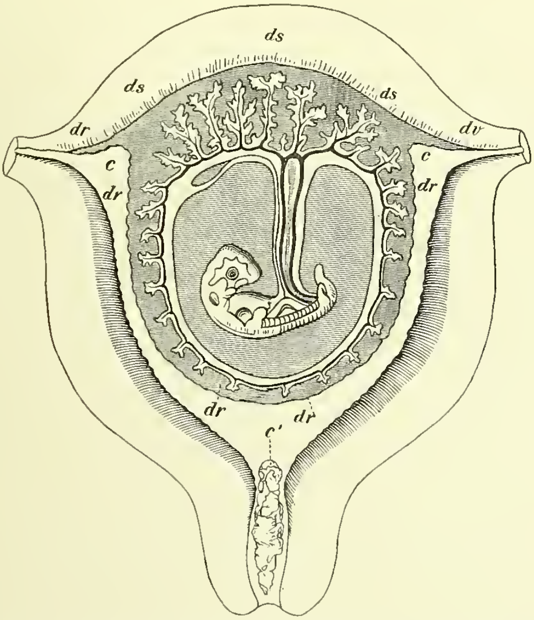
The Placenta is composed of the serotine decidua with its large venous sinuses through which the maternal blood circulates; of the chorion and amnion with the fœtal arteries and vein. In the placenta the maternal and fœtal blood come into relation. There are three tissue layers between the fœtal and maternal blood. The epiblast and somatopleure of the villus and the endothelium of the capillaries. Through these fissures the fœtus receives nourishment from the maternal organism.

8. THE PHYSIOLOGY OF THE EMBRYO AND FŒTUS.

a. Nutrition.

1. **Foods, Digestion and Absorption.**—The origin of the animal individual from an ovum is practically universal, (protozoa excepted, perhaps). The fertilized ovum consists of the minute segmentation-nucleus and the yolk-mass which represents the first installment of maternal nourishment. The yolk-mass is relatively large in birds and reptiles and relatively small in mammals.

Fig. 339.



Diagrammatic view of a vertical transverse section of the uterus at the seventh or eighth week of pregnancy. *c*, *c*, *c′*, cavity of uterus, which becomes the cavity of the decidua, opening at *c*, *c*, the cornua, into the Fallopian tubes, and at *c′* into the cavity of the cervix, which is closed by a plug of mucus; *dv*, decidua vera; *dr*, decidua reflexa, with the sparser villi imbedded in its substance; *ds*, decidua serotina, involving the more developed chorionic villi of the commencing placenta. The fœtus is seen lying in the amniotic sac; passing up from the umbilicus is seen the umbilical cord and its vessels passing to their distribution in the villi of the chorion; also the pedicle of the yolk-sack, which lies in the cavity between the amnion and chorion. (Allen Thomson.)

(*a*) Birds may be taken as an example of those animals whose embryos are provided with a large yolk-mass. The hen's egg weighs 50 gms., of which 5 gms. is shell and 45 gms. food. The white weighs 30 gms. and consists of *proteids* (albumins and globulins) 3 gms., *fats* 0.3 gms., *salts* 0.1 gms., *water* 26.6 gms.

The YOLK weighs 15 gms. and consists of *proteids*, 1.7 gms., *fat* 3 gms., *vitelline, nuclein, glycogen* 0.2 gm., *Lecithin* 1 gm., *salts* 0.1 gm., *water* 9 gms. The salts contain bone-making material,—phosphates and carbonates,—also blood and tissue constituents,—chlorides, phosphates and carbonates.

The chicken from a 50-gm. egg weighs 35 gms., 10 gms. having been lost in katabolism, and passed through the pores of the shell as CO_2 and H_2O. The small amount of nitrogenous excreta remains within the shell, generally within the cloaca of the chick to be voided soon after it leaves the shell. The chicken is 80 per cent. water (28 gms. water and 7 gms. solids), while the egg is 79.1 per cent. water.

(*b*) MAMMALS present a more complex problem. The mammalian ovum has a small proportion of yolk and is retained within the uterus of the mother long after this meager supply is exhausted. After the yolk-mass is exhausted the embryo "takes root" in the maternal tissues and draws plasma and oxygen from the mother. The mammalian mother furnishes her intra-uterine offspring with two sources of food the *yolk-mass* and her own *blood*. Besides this there is a special provision for the extra-uterine period when the young mammal is more or less helpless; viz., the *milk* which the mother secretes.

(*α*) *The Yolk-mass* probably has about the same chemical composition in the mammal as in the bird. This yolk-mass must be *digested*. It is surrounded by the hypoblast which is to furnish the epithelium of the alimentary tract. There are no glands to secrete a digestive fluid at the period when the yolk is consumed, yet the yolk can be absorbed only after solution. The hypoblastic cells lining the yolk sac and cœlenteron must digest and absorb the yolk-mass. In this connection it must not be forgotten that the white of the bird's egg is outside of the epiblast of the chorion and must be absorbed by the chorion. In the mammal the epiblast of the chorion is the principal absorbing surface.

(*β*) *The maternal blood* is the source from which the mammalian fœtus draws sustenance. The special organs involved in this process have been mentioned above. Maternal red corpuscles do not pass into the fœtus. Maternal white corpuscles probably do pass from maternal to fœtal circulation. It is easy to see how all soluble salts can readily pass from maternal to fœtal plasma and the effect of various drugs upon the fœtus when given to the mother demonstrate that they do pass from one to the other. Just how plasma-proteids pass from the mother to the fœtus is a puzzle still unsolved. Some have suggested that the maternal plasma-proteids are peptonized, diffuse through the dividing membranes, and changed back to proteid; others think the white corpuscles carry proteid from mother to young.

Toward the end of intra-uterine life the mammalian fœtus swallows a portion of the amniotic fluid. The amount of amniotic fluid is very small at first, but increases progressively with the period of gestation. This fluid diffuses or filters into the amniotic sac from the maternal, and, perhaps, fœtal lymph spaces. It contains water (an important constituent of embryonic tissue) and various salts with small portions of other foodstuffs.

2. **Circulation.**—(*a*) The Circulation of the Embryo is the *vitelline circulation* or the system of vessels which spread over the yolk beginning with the area vasculosa. The principal arteries are the paired vitelline arteries which pass out on either side branching profusely as far as the vena terminalis. From the vena terminalis or terminal sinus a system of venules and veins brings the blood back to the venous sinus, from which it passes into the heart.

(*b*) The Circulation of the Fœtus, "*Fœtal Circulation*," a diagram of which appears above (Fig. 320), is a special adaptation of the permanent circulation. The permanent circulation sends the blood to the lungs for oxidation of the hæmoglobin, but the fœtal lungs not being functional there is a means provided to direct the blood stream from them. This necessitates two important structures peculiar to the fœtus: (I) The *foramen ovale* through inter-auricular septum; (II) the *ductus arteriosus* from the pulmonary artery to the arch of the aorta. Other peculiarities of the fœtal circulation are: (III) the *hypogastric arteries* which carry impure blood from the iliac arteries to the umbilical arteries through which it passes to the placenta for oxidation of the hæmoglobin; (IV) The *ductus venosus*, from the umbilical vein to the vena cava, which provides for the direct passage of a large portion of the pure blood to the left side of the heart through the foramen ovale. The four structural peculiarities of the fœtal circulation, lead to the following functional peculiarities: (I) the circulation of venous blood in the hypogastric and umbilical arteries; (II) of arterial blood in the umbilical vein and ductus venosus; (III) of arterial blood in the ascending vena cava, mixed, however, with venous blood from the lower extremities; (IV) of the mixed blood (the purest which enters the heart) in the arteries of the head and anterior extremities; (V) of the least pure blood,—further mixed with the blood from the ductus arteriosus,—to the posterior extremities and the placenta.

3. **Respiration.**—In birds and reptiles the respiration takes place readily through the porous shell, and shell-membrane, the vitelline arteries bringing the impure blood from the body of the embryo out upon the surface of the yolk. If the shell be varnished the chick will smother.

In mammals the respiration is carried on through the placenta.

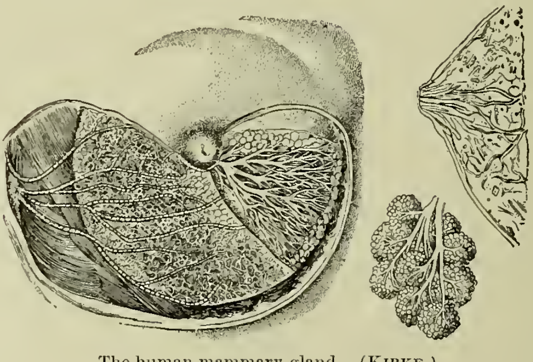
The blood of the fœtus is brought into relation with the maternal blood. The oxygen pressure in the fœtal blood is much lower than that in the maternal blood, so that the oxygen passes readily from maternal to the fœtal blood through the dividing membranes.

4. **Metabolism and Excretion.**—In the parasitic life led by the embryo and fœtus the anabolic processes are greatly in excess of the katabolic processes. The food is presented to the fœtus so nearly ready for assimilation that almost no energy is consumed in preparation of the food. This food must be transported, however, and this transportation by the circulatory system involves the liberation of kinetic energy of mechanical motion. This energy can be liberated only through katabolism of embryonic tissues and fluids. The katabolites are for the most part CO_2 and H_2O, but some nitrogenous compounds (urea, etc.) are formed, and these must be thrown out of the body of the embryo. At an early period of fœtal life the mesonephros—later the metanephros or permanent kidney—becomes functional and excretes urea, etc., which finds its way out of the cloaca or of the bladder, and enters the amniotic fluid. The amniotic fluid—as stated above—may be swallowed by the fœtus during the later stages of intra-uterine life. This accounts for the presence of urea in the alimentary tract of the newborn.

b. Moto-Sensory Activity.

That the fœtus is conscious of any sensation is not even remotely probable. That the fœtus responds reflexly to various stimuli is beyond question. The "quickening," which takes place at the middle of the period of intra-uterine life is the beginning of general body movements. From the first quickening to within about a week of delivery the movements increase in frequency, strength and evident reflex character.

Fig. 340.



The human mammary gland. (Kirke.)

9. THE PHYSIOLOGY OF MATERNITY.

a. Pregnancy and Parturition.[1]

b. Lactation.

The milk-secreting glands are cutaneous, and the glandular epithelium is epiblastic in origin. The accompanying figure gives the most important anatomical features of the mammary gland. (Fig. 340.)

FIG. 341.

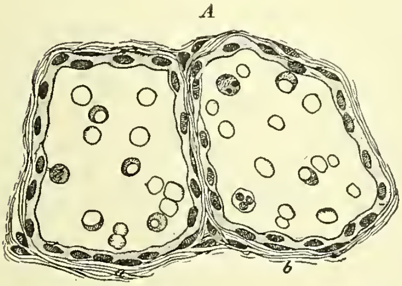
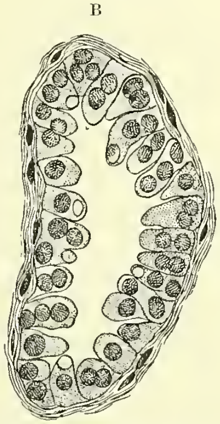


FIG. 342.



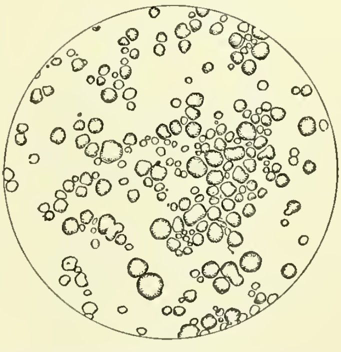
Alveoli of the mammary gland of the bitch under different conditions of activity. *A*, section through the middle of two alveoli at the commencement of lactation, the epithelial cells being seen in profile ; *B*, an alveolus in full secretory activity. (SCHAEFER after HEIDENHAIN.)

The secretion of the milk is analogous to the secretion of the oil of oil glands in that the cellular elements of the gland-epithelium are sacrificed in the process. Figures 341 and 342 show the glandular alveoli under different stages of activity.

Milk has, under the microscope the appearance shown in Fig. 343. The corpuscular elements are either colostrum corpuscles, or casein-pellicled oil globules.

Milk is a physiological emulsion and has the chemical constitution shown in the following table :

FIG. 343.



Globules and molecules of cow's milk. × 400. (KIRKE.)

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[1] These topics though properly in the field of physiology are extensively discussed in works on obstetrics. They need not be taken up here.

COMPOSITION OF HUMAN MILK.

Water	902.717
Casein (desiccated)	29.000
Lacto-protein	1.000
Albumin	....
Butter	25.000
Sugar of milk	37.000
Sodium lactate	0.420
Sodium chloride	0.240
Potassium chloride	1.440
Sodium carbonate	0.053
Calcium carbonate	0.069
Calcium phosphate	2.310
Magnesium phosphate	0.420
Sodium phosphate	0.225
Ferric phosphate	0.032
Sodium sulphate	0.074
Potassium sulphate	....
	1000.000

Gases in solution	Oxygen	1.29	30 parts per 1000 in volume.
	Nitrogen	12.17	
	Carbonic acid	16.54	

Milk contains food for the teeth and food for the bones, food for the muscles and food for the nervous system. It is a perfect food, satisfying every need of the developing infant.

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